10.21608/AVMJ.2025.328197.1435 Assiut University web-site: www.aun.edu.eg

ROLE OF ESTROGEN ON THE ORAL TISSUE INTEGRITY

ATEF I. AHMED [1]; FIRAS D. ALSOLEIHAT [2];
MAHMOUD A. ATTIA [3] AND AHMED M. HUSSEIN [4]

[1] Professor of Oral Biology, Department of Restorative Dentistry and Basic Medical Sciences, Faculty of Dentistry, University of Petra, Amman, Jordan; and Faculty of Oral Medicine, Al-Azhar University (Assiut Branch), Egypt.

[2] Professor and Head of Department of Restorative Dentistry and Basic Medical Sciences, Faculty of Dentistry, University of Petra; and Department of Restorative Dentistry, School of Dentistry, University of Jordan, Amman, Jordan.

[3] Department of Oral Pathology, Faculty of Oral Medicine, Al-Azhar University (Assiut Branch), Egypt; and Faculty of Applied Medical Science, Al-Baha University, Saudi Arabia.

[4] Associated Professor of Oral and Maxillofacial Pathology, Faculty of Dentistry, University of Petra, Amman, Jordan; and Faculty of Dentistry, Assiut University, Assiut, Egypt.

Running Title: Estrogen in Oral Health

Received: 21 November 2024; **Accepted:** 30 December 2024

ABSTRACT

The oral cavity is comprised of several structures that have different functions and reflect the overall health. Sex hormones are steroids produced from cholesterol. They are secreted in the mouth with saliva that is thought to possess some healing properties. Many studies have been aimed at the impacts of hormone fluctuations on certain types of oral tissues, especially periodontal tissues. There are numerous changes experienced as a result of hypoestrogenism among them being oral alterations. Local changes include a reduction of salivary function leading to decreased salivation and a predisposition of the oral mucosa to ulceration. Also in the oral cavity, xerostomia may make tooth caries more frequent. Added to the reduction of saliva, the gingival epithelium also becomes less robust, thus may further result in increased tooth mobility and possibly tooth loss due to the risk of invasion by bacteria and reduced alveolar bone mineral density for bone resorption. Since periodontal disease is one of the things that lowers quality of life, prevention and treatment of this damage are needed. To locate studies that address it, the main question to search for is: “Has there been any relationship between the concentration of estrogen in the body fluids and the integrities and healthy status of the oral tissues?". This review revealed that the balance of the body's estrogen hormone with the periodontium is fixed. The objective of the present search was to establish whether intact and healthy oral tissues are linked with sex hormones within body fluids. So the dentist has a good understanding of hormonal changes in women, and how they affect gingival diseases.

Keywords: Estrogen, Periodontal Tissue, Oral Health, Oral Tissue Integrity, Sex Hormones

Corresponding author: Ahmed M. Hussein
E-mail address: ahmedattay@dent.aun.edu.eg
Present address*:* Associated Professor of Oral and Maxillofacial Pathology, Faculty of Dentistry, University of Petra, Amman, Jordan; and Faculty of Dentistry, Assiut University, Assiut, Egypt.

INTRODUCTION

In multicellular animals, hormones are chemical messengers that coordinate behavior and physiological response by emitting a signal for a distant organ with the help of complicated biological pathways *(Huang L et al., 2024).* These hormones regulate digestion, metabolism, breathing, sleeping, excretion, lactation, development and growth, sexual activity, and feelings. The hormones get to the distant cells through the bloodstream via binding receptor proteins on the target cell; this leads to signal amplification which normally triggers gene synthesis to produce more of the target proteins *(van den et al., 2018, Iwobi et al., 2023).* In the field, the rate of secretion and biosynthesis of hormones is controlled by a negative feedback homeostatic mechanism (Figure 1). This mechanism depends on a factor that affects the hormones' production and elimination. Thus, a greater hormonal concentration is not enough to draw negative feedback. Nevertheless, it is stimulated by the increased formation of an "effect" of the hormone *(Johnstone et al., 2014).*

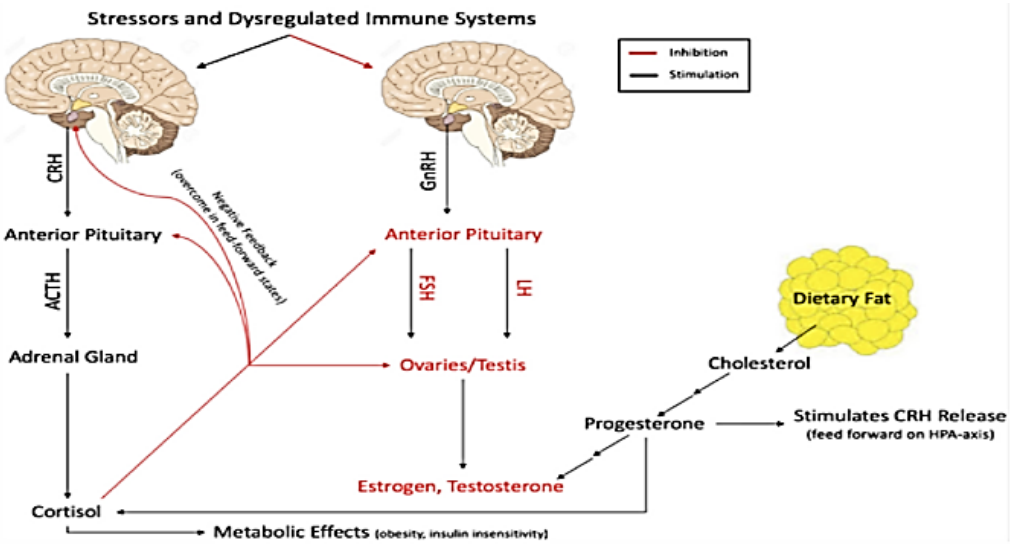

Figure 1: Flow diagram of the interaction between the hypothalamic-pituitary axis and sex hormone productions (Abe *et al.*, 2023).

The gonads produce sex hormones as the result of the biochemical conversion of other steroids (Figure 2) that are present in the liver or adipose tissue *(Abaffy et al., 2023).* Sex hormones are also called sex steroids or gonadotropic hormones, gonadal hormones or gonad corticoids *(Pompili et al., 2020).* The class of hormones associated with female sexual development is estrogen. Testosterone is the sex hormone produced by the testicles and is termed an androgen. They mainly act to bring about sexual dimorphism and sex as it were. In the scenario outlined by the authors, these hormones impact through slow-rate genomic steroid mechanisms involving nuclear receptors and non-genomic steroid mechanisms involving membrane-bound receptors to initiate a variety of signalling pathways in a fast response (Forsyth *et al.*, 2024). Luteinizing hormone, follicle-stimulating hormone, and gonadotrophic releasing hormone relate to the sex hormones and activate sex-regulated effect yet, are themselves not classified as sex hormones (Hanssen, 2021).

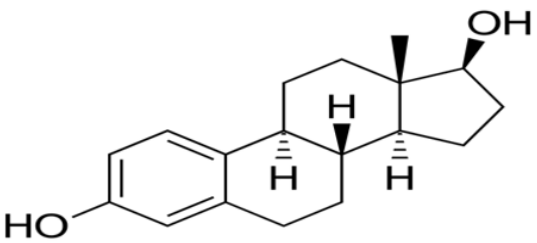

Figure 2: The structural biology of estrogen (Thomas *et al.*, 2013).

Many different species of life can synthesize and transport sex steroid hormones; bacteria, plants, parasites, and mammals. Mammals' testes, ovaries, adrenal cortex, and placenta during pregnancy all secrete sex hormones, created from cholesterol *(Tarkowská, 2019, Buendía-González et al., 2022).* After secretion, they circulate through the bloodstream and reach the target tissues where they facilitate several physiologic functions *(Wang et al., 2023).* One might notice an important fact; there is the same structure but different reactions of sex steroid hormones in their target tissues. The impact of these chemicals does not bypass the mouth. These molecules have the characteristic of penetrating diffusion in the salivary glands ducts and blood arteries. So they are capable of invading tissues within the mouth such as the periodontium and elicit a response there. Numerous scholars have endeavoured to elucidate the reasons for the alterations in oral health, the mechanisms implicated, and the potential consequences for the host. Four distinct pathways have been postulated by researchers to explain how sex hormones influence periodontal tissues and the environment around them: by (1) making alterations in the conformation and activity of localized epithelial cells and fibroblast; (2) increasing capillary permeability; (3) increasing leukocyte and lymphocyte concentration in the periodontium; and (4) inducing changes in certain oral microorganisms *(Alanazi et al., 2024).* Studies on the relationship between sex steroid hormones and mouth bacteria and fungi by various authors still produce contradictory evidence *(Manos, 2022).*

Estrogen is secreted into the bloodstream by the ovaries and other tissues. Once in the bloodstream, estrogen can be transported to the salivary glands. It is a lipophilic molecule that can cross cell membranes relatively easily. When estrogen enters the bloodstream, it can also diffuse into the salivary glands. The salivary glands can filter substances from the blood. The estrogen in the bloodstream is secreted into the saliva by passive diffusion. This means that the concentration of estrogen in the saliva will generally mirror its levels in the blood, though it may be at a lower concentration due to the filtering process. The presence of estrogen in saliva is influenced by its level in the bloodstream. During periods of high estrogen, the concentration of estrogen in saliva will also be higher. Conversely, during times of low estrogen as in postmenopausal women, the concentration in saliva will be lower *(Handajani et al., 2020).*

AIMS

The current review was designed with an emphasis on the relationship between changes in estrogen sex hormone and the integrity and health of oral tissues at different women's ages. Furthermore, knowledge about how this hormone affects oral health was evaluated.

METHODS

The electronic databases; Scopus, PubMed, Google Scholar, and Research Gate were searched for scientific papers for the current literature review. The search phrases "Sex Hormones," "Periodontal Health," "Periodontal Disease," "Estrogen," "Testosterone," "Oral Health," and "Hormones" were used, along with their combinations.

LITERATURE REVIEW

I- Menopause and its Effects

Menopauseis a physiological occurrence that occurs between 45 and 55 years, it marks the cessation of menstruation and the end of a woman's fertility. Due to the decline of ovarian function, the changes that occur after menopause are not the same as those that occur during pregnancy. Women's sex hormones change dramatically during the menopause phase of their lives. Fluctuations in average FSH mean that although estradiol will decrease for at least 2 years, FSH will increase. This is a very important player in responding to the effects on the orofacial tissues *(Rogowska et al., 2023).*

1. Xerostomia: xerostomia is among the most common postmenopausal complaints in women. This disorder is caused by decreased salivary flows or by regular salivary components with less and less concentration. Dry mouth due to medicines, alcohol or tobacco, and poor oral hygiene create a slick for the material that thickens plaque at the surfaces of the dentures and teeth it covers. It is a condition which raises the susceptibility to both caries and periodontal disease *(Ciesielska et al., 2022).*

2. Dental caries: hypo-salivation is associated with various complications such as raised tooth cavities, dysphagia, taste perversion, oral infections, and raised mucosal sensitivity to mechanical stress. Furthermore, bacteria require a wet environment to colonize and reproduce actively in the mouth, low salivary secretion could disrupt the population of such microbes that promote strepto mutans and candida albicans *(Villalobos et al., 2022, Agrawal et al., 2022).* Due to increased salivary secretion by postmenopausal women on hormone therapy, their quality of life is improved. The composition of saliva in the women appears to be dependent on estrogen levels. At the same time, hormone therapy does not affect the number of bacteria in the saliva of either premenopausal or postmenopausal patients *(Mary et al., 2022).* Rukmini and colleagues have suggested that there are disparities in dental caries that exist between premenopausal and postmenopausal women for which a decreased salivary flow in postmenopausal women encourages microbial accumulation thereby increasing the tooth caries *(Rukmini et al., 2018).*

3. Periodontium Changes: Postmenopausal women are more prone to periodontal disease; this is brought on by an estrogen shortage, which also results in bone resorption and gingival inflammation. The periodontium contains both androgen and estrogen hormones, therefore any hormonal abnormalities will have an impact on the periodontium. The ecology of oral cavity bacteria and immunological function are altered by hypoestrogenism *(Bianchi et al., 2020)* Changes in the width of capillary loops, blood vessel tortuosity in the labial mucosa, and variations in the density of the periodontal mucosa predispose to periodontal inflammation were seen in the microcirculation of the postmenopausal oral tissues. Alterations in the anti-inflammatory cytokines may result from the rise in postmenopausal pre-inflammatory cytokines. This results in a decline in monocyte and macrophage function *(Di Naro et al., 2021).*

3.A. Gingiva: estrogen has the potential to induce gingival fibroblast proliferation and gingival lamina propria descent. In addition, it stimulates the growth of cells in the blood vessels and the gums. Estrogen priests the epithelial barrier to become thinner or shrinks the epithelial barrier owing to increased glycogen content and decreased keratinization. Things such as the absence of T cells, low leukocyte count, high phagocytosis, low chemotaxis, and cytokines that the bone marrow produces when it is inflamed, resulting in estrogen-induced inflammation *(Yang et al., 2022).* The possible pathways have been presented to explain how the estrogen hormone affects gingival cells: However, altering the resistance of the epithelial barrier to bacterial invasion as well as collagen maintenance and repair *(Boyapati et al., 2021).* Adam's study shows that the estrogen hormone modulates target tissue cell development, differentiation, and proliferation, such as gingival keratinocytes and fibroblasts *(Adam et al., 2022).* In contrast, other findings suggested that the estrogen does not influence the collagen that gingival fibroblasts synthesize *(Jafri et al, 2015).*

3.B. Cementum: it has been noted that going through menopause is accompanied by changes in the activity of alkaline phosphatase that supports cementogenesis. Postmenopausal changes in alkaline

phosphatase also affect the periodontal status particularly cementum as extremely high alkaline phosphatase activity was recorded during the acellular cementum apposition *(Hutomo et al., 2021).*

3.C. Periodontal Ligament: it should be noted that one of the elements that regulate the periodontal tissue, is the ability of undifferentiated mesenchymal cells of the periodontal ligament to transform into osteoblasts, cementoblasts, and fibroblasts. The estrogen receptors regulate the osteoprotegerin and receptor activator of nuclear factor kappa-B, which plays massive roles in etiology, presentation, and progression in the periodontal ligament cells when estrogen is deficient *(Nastri et al., 2020).* The primary role of the sex hormone estrogen is to initiate the development of periodontal ligament stem cells and to inhibit bone resorption after a woman reaches menopause (Figure 3). Further, collagen synthesis, osteogenic and osteoblastic differentiation in the periodontal ligament are also lowered *(Park et al., 2022).*

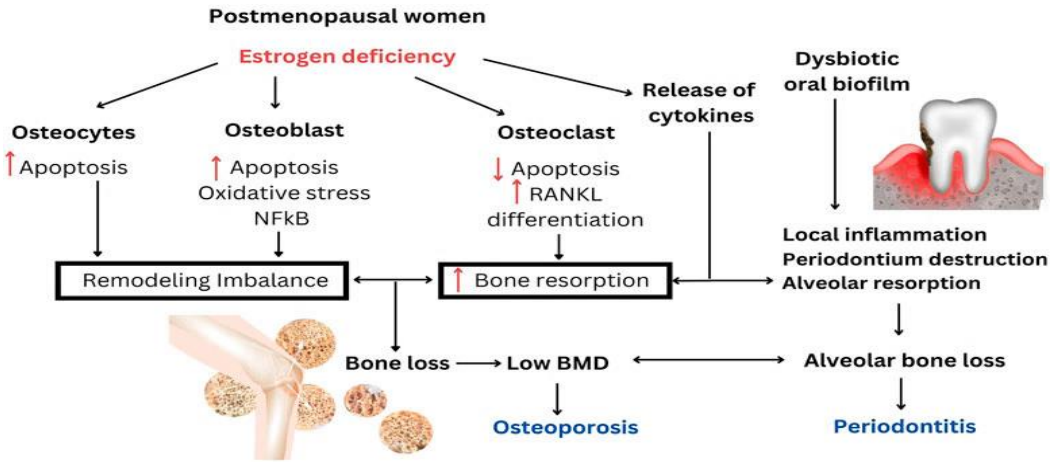

Figure 3: Overview of postmenopausal osteoporosis and periodontitis (Jayusman *et al.*, 2023).

3.D. Alveolar Bone: the synthesis of interleukin 1(IL-1), IL-6, IL-8, IL-10, and tumor necrosis factor-alpha, granulocyte colony stimulant, and macrophage stimulant are associated with estrogen deficiency after menopause and stimulates the osteoclast and increases bone resorption. However, the causes of toothlessness are not very simple, but they are an indication of the general status of oral health over time *(Yakar et al., 2021).* Decreased secretion of estrogen leads to a decrease in bone remodelling Alveolar bone resorption rises due to inhibition of the positive feedback of the hypothalamic-pituitary axis to the ovary. The deficiency of estrogen in postmenopausal backup most ordinarily leads to osteoporosis. Tooth loss occurs with deteriorating alveolar bone status higher in osteoporosis and can be concluded with higher resorption rates. Based on findings of high cytokine levels, low bone density, and high bone turnover rates by menopause, periodontal disease might be considered pre-disposed. This of course raises the prospect of periodontal disease predominantly affecting females *(Cecoro et al., 2021).*

4- Burning Mouth Syndrome: is a common problem for women to experience oral discomfort during their various stages of menopause. It is one of the common complaints in premenopausal and postmenopausal women. This syndrome may be described as burning of the mucosa of the mouth, with or without dryness of the mouth and taste perversion. Estrogen deficiency

leads to epithelial immaturity resulting in atrophic epithelium and hence to burning mouth complaints because of inflammation *(Sumit et al., 2024).* Estrogen inhibition is a phenomenon associated with female complaints of burning sensations in the mouth and tongue. Some females may be affected by menopausal gingivostomatitis, a condition characterized by dry, shiny gingiva which is easily bleeds and its color changes from pale to erythematous *(Yakar et al., 2024).*

Therefore, the matter is arguable that while few women would normally develop oral manifestations after menopause, some of them do partly as the example of menopausal gingivostomatitis (Figure 4). It is characterized by a shiny, dry lining of the mouth and lips and the reddish pink oral mucosa which may look lighter in color or have a bright red hue and are inclined to tear easily. The more often described gingival changes in female patients of this age are the desquamative type with mottled coloration and well-polished gingival smear. On the contrary, due to multifactorial causation, it is difficult to associate sex hormones with the pathophysiology of the disorder *(Sumadhura et al., 2018).*

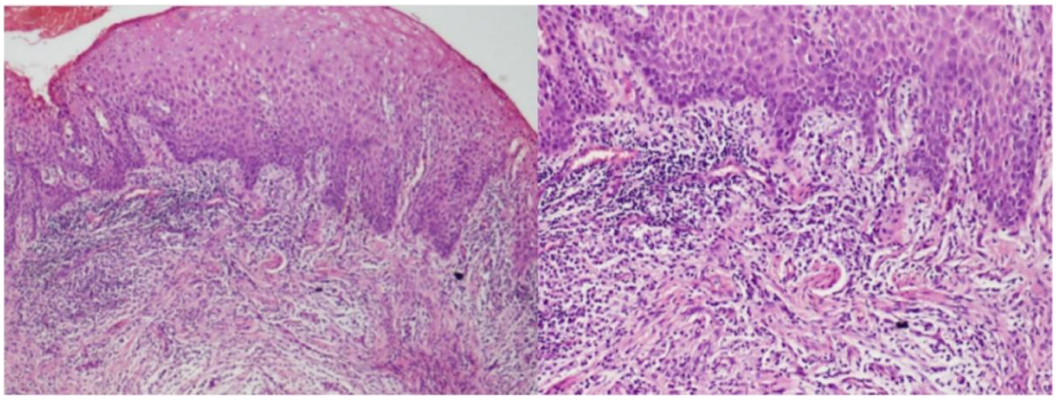

Figure 4: H&E-stained specimen revealed para-keratinized epithelium with inflammatory cell infiltrate in the connective tissue suggestive of gingival hypertrophy (Sathish *et al.,* 2022).

The one that was mentioned most often during the menopausal phase is that there is a particularly high risk for osteoporosis to occur. Estrogen deficiency affects total bone remodeling and the general regulation of collagen synthesis. Forces described by the authors as postmenopausal osteoporosis, causing low bone mass, bone mineral density and bone strength and increased risk of fractures affect 33% of women above the age of 60 years. Bones in postmenopausal women have been observed reduced in mass, density, and mineral content; the mandible is more affected than the maxilla, and the changes are in proportion to the aging process *(Leucuta et al., 2024).* While this relationship is contentious, postmenopausal women may be at greater risk of developing periodontal diseases because they are more vulnerable to developing osteoporosis. Reduced alveolar crest height and tooth loss are evidence that osteoporosis and periodontal disease are positively related *(Kim et al., 2024).*

In summary, the significant oral changes during postmenopause related to hypoestrogenism; are xerostomia, gingivitis, periodontal disease, thinning of oral tissues, and changes in oral mucosal health. Premenopausal women may experience some fluctuations in oral health tied to their menstrual cycle and hormonal changes, but the effects are generally less pronounced compared to postmenopausal women (Table 1) (Figure 5).

Table 1: Summary table contrasting pre- and postmenopausal changes in oral tissues.

Feature	Premenopausal	Postmenopausal
Salivary flow	Normal saliva flow	Xerostomia
Gingiva	Temporary gingivitis occurs during menstruation	Increased risk of gingival diseases
Bone Density	Normal.	Decreased
Oral Mucosa	Healthy mucosa	Thinner, more fragile mucosa
Taste Sensation	Normal	Dysgeusia
Tooth Sensitivity	Normal	Increased
Periodontal Disease	Temporary periodontitis during hormonal changes	Increased risk of periodontal disease
Temporomandibular Joint (TMJ)	No significant changes in the TMJ	Increased risk of TMJ disorders

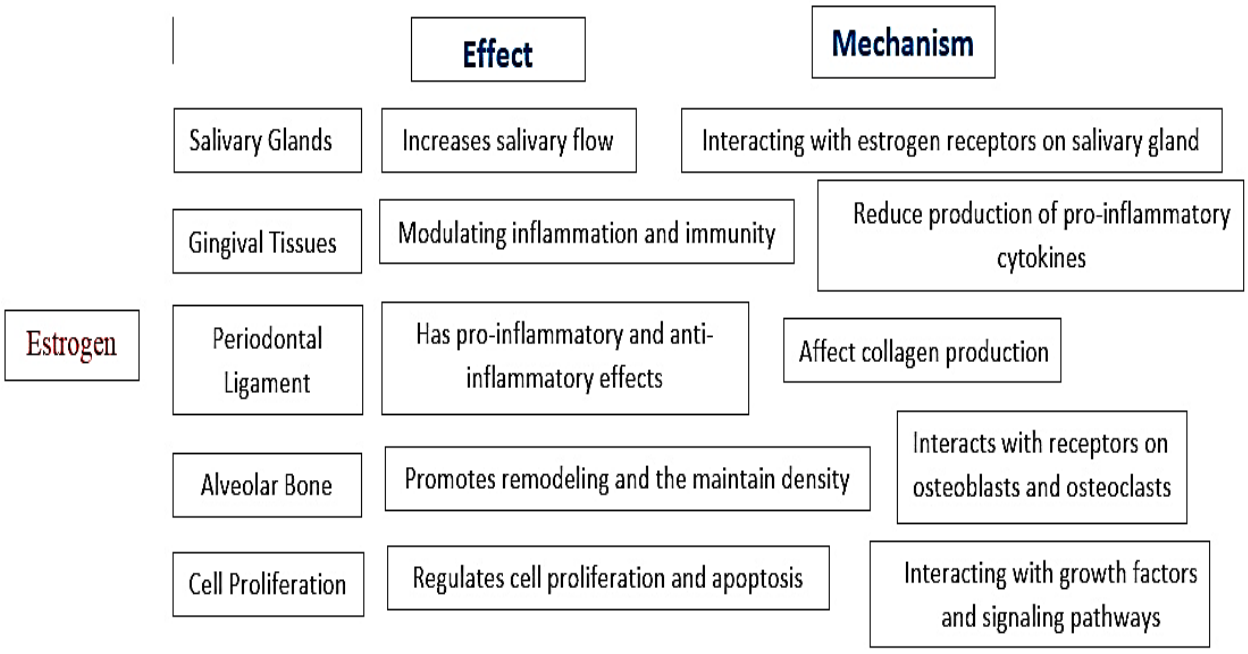

Figure 5: The main effects of estrogen in oral tissues with reference to the main mechanisms.

II- Puberty and its Effects

The puberty is characterized by changes in behavior, the development of secondary sex characteristics, and a demonstrative increase in the levels of estrogen hormone. Puberty triggers changes in the periodontium and an increase in the incidences of gingivitis then regression during adolescence. Puberty gingivitis includes exuberant inflammation, and gingival overgrowth which may be associated with gingival bleeding. What is worth appreciating is that gingival inflammation may not go hand in hand with the levels of plaque but may well have a direct relation with hormonal levels *(Qi et al., 2023)*. The microbial changes noted occur during this age are attributed to a response of the gingival tissue to sex hormones that change its microflora. Furthermore, some species of bacteria are capable of benefiting from the higher dose of hormones which is normally present *(Penoni et al., 2017, Niramitchainon et al., 2020)*.

III- Menstrual Cycle and its Effects

The initiation of estrogen and progesterone production and release in a cyclic pattern as associated to puberty defines the menstrual or reproductive cycle. Disruptions of sex hormones have been proven to worsen severe gingival inflammatory changes. Swelling which developed pink with hemorrhagic niches during the premenstrum was the distinguishing feature of 'Mühlemann's gingivitis intermenstrualis." Because hormonal imbalances affect the gingival tissue and cause changes in the gingival crevicular fluid during menstruation, individuals with certain gingivitis develop them more than those with sound gingiva. In addition, changes in the inflammatory cytokines including IL-1β have also been well documented to increase steadily in gingival crevicular fluid from the early follicular phase, the day of menstruation to the peak progesterone day. This may be due to its capacity of promoting inflammatory cells to release proportionately more IL-1β, according to its high concentration. These other inflammatory cytokines include IL-6 and tumor necrosis factor alpha or gamma possibly at different concentrations and ratios that also contribute to the inflammatory changes noticed in the gingiva throughout the menstrual cycle. (Savić *et al.,* 2017, Sumbayak *et al., 2023)*

IV- Pregnancy and its Effects

Estrogen and progesterone are the 2 hormones that play a central role during pregnancy. Periodontium may cure pathological disorders like infected gums, pregnancy tumors, periodontal disease, and caries of the teeth at this interesting stage. Pregnancy gingivitis, which may be non-specific, vascularizing, proliferative, and inflammatory with increased cell infiltration affects between 35-100% of pregnant women. It starts in the second month of pregnancy and lasts until the eighth, with the first and second trimesters having the greatest impact *(Chen et al., 2022).* Another common oral finding is tooth movement, including changes in probing pocket depths which could seemingly be worse due to edema or hyperplasic gingival changes (Dassatti *et al., 2019).* Also, the supra and sub-gingival microbiota shifts have been identified (Balan *et al.,* 2018). Besides pregnant women were described as having changes in certain immune-regulatory cytokines, including T cells. An acute inflammatory response to plaque is avoided due to the active hormone buildup in the gingival layer and increased immunity suppression by active hormone. Hence, there is a chronic type of inflammation that occurs, thereby making a show of inflammation in the gum as a result even more apparent *(Huang et al., 2020).*

The state of periodontal disease during pregnancy reflects the effect of progesterone through microbial action, raised levels in the gingiva, and immunosuppression. Concentrations of sex hormones in saliva can change the oral microbiota and oral environment, which in turn triggers a reaction from the host. Among these changes are the spread of certain species and the conversion of estrogen hormone into different compounds through metabolism. As this is going on, the host reacts to these modifications by metabolizing estrogen hormone in the medium and adjusting its physiological response to the surrounding circumstances (Figure 6) (Cornejo *et al.* 2019). In the first or second trimester a red, swollen gingival lesion, a pyogenic granuloma sometimes called a pregnancy tumor, or epulis gravidarum may develop. While clinically and histologically, it appears to be like any pyogenic granuloma, this proliferative lesion may develop in a variety

of situations such as trauma, deranged hormone levels, and plaque. These may be due to these compounds' effect on the overall immune response, the gingival vasculature, and the inhibition of collagenase by progesterone. After delivery, the lesion either resolves or persists as a fibrous mass after birth. However, some of them could be painful; take time to stop bleeding or suppurate; and make it thoroughly uncomfortable to chew food (Ozgen *et al.*, 2021).

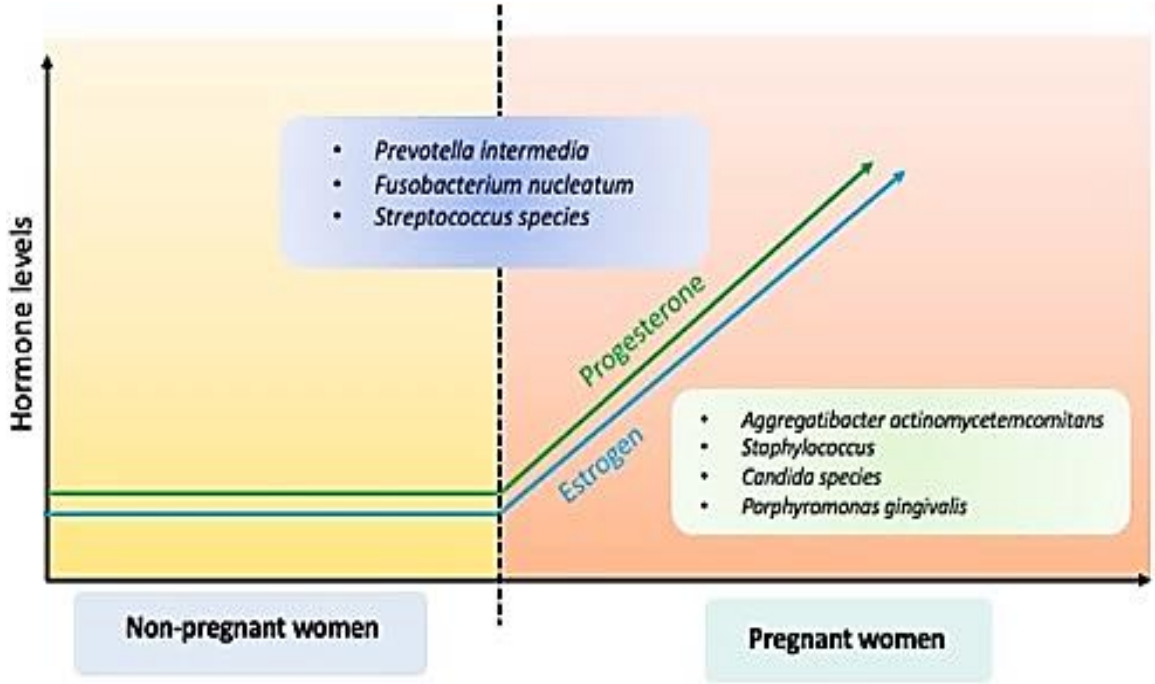

Figure 6: Oral microbiome and pregnancy: a bidirectional relationship (Saadaoui *et al.*, 2021).

V- Oral Contraceptives and their Effects

The medicine class that is most often used worldwide is the oral contraceptives. At the beginning of the 1960s, the level of estrogen in oral contraceptives used to be very high and this has led to so many systemic side effects such as cancer and cardiovascular diseases. The current quantities are considerably smaller and contain low amounts of progestins (1.5mg/day) and/or estrogens (0.05 mg/day); {1 mg norethisterone acetate + 0.05 mg ethinylestradiol/mestranol}. When taking these medications, they enhance the effect of progesterone and estrogen on the periodontal tissues. Some of the documented changes of oral contraceptives on the periodontium include hyperplastic gingivitis, marked gingival exudate and inflammation had been reported (Rojo *et al.*, 2024). As with most other pathological changes, those on the gingival tissues are dose and time-dependent. Further, even after three years of use, oral contraceptives appear to influence some Candida species that were able to survive the conditions caused by sex hormones. These drugs also affected the alveolar bone beneath the gingival tissue (Prachi *et al.*, 2019).

Nevertheless, there's evidence to show that long-time utilization of oral contraceptives is also positively reinforcing bone metabolism in the body. Specifically, in the elevated mean bone mineral density and the lowered serum levels bone biomarkers such as alkaline phosphatase imply long duration oral

contraceptive users are less likely to suffer from osteoporosis. In a specific concern, some researchers suggest that women who use modern oral contraceptives are not allergic to gingival inflammation, which is different from the inflammatory changes in the gingival tissues produced by oral contraceptives observed in studies before. However, local abrasive agents may cause exaggerated responses from the gingival tissues *(Beksinska et al., 2018, Kim et al., 2022).*

Although oral contraceptives are not used for delaying puberty, they may affect the puberty time when prescribed in some cases like severe dysmenorrhea or abnormal hormonal regulation. There is some evidence to suggest that starting oral contraceptives in early adolescence can affect growth and pubertal development. However, this impact is generally considered minimal if the woman is already in mid-to-late puberty. Oral contraceptives primarily function by delivering synthetic forms of estrogen and/or progestin to prevent ovulation, thicken cervical mucus, and change the endometrial lining. Their effectiveness is largely due to their ability to maintain consistent hormone levels in the body, which suppresses the natural cyclical hormonal fluctuations. It has been shown that oral contraceptives are more effective when used correctly, with typical use rates showing a pregnancy prevention rate (Sanfilippo *et al.*, 2009).

VI- Polycystic Ovary Syndrome

Currently, there are precise diagnostic criteria for the most specific subtype of the renal-gut axis metabolic syndrome in line with the National Institutes of Health, and it is polycystic ovary syndrome (PCOS). This pathology affects 6.5-8% of women of reproductive age. Further, women with PCOS have insulin resistance and central obesity, dyslipidemia, and cardiovascular risk assessment. Among many disorders, these systemized diseases have also been associated with periodontal diseases. PCOS and periodontal diseases have been established to be associated with increased oxidative stress and amplified inflammatory cytokines including IL-6 and C-reactive protein. These results may suggest that both illnesses may be due to a similar disease process, in terms of pathophysiology. In this cross-talk, sterile PCOS inflammatory milieu is manifested by increment in pro-inflammatory cytokines like IL-6, IL-17, and tumor necrosis factor-alpha and gingival inflammation concomitantly. However, there is a bidirectional relationship between PCOS and gingival inflammation. However, the destructive and inflammatory process may not occur without a general systemic inflammation (Guan *et al.*, 2022).

Gingival inflammation and oral microbes may also be influenced by PCOS as it changes the composition of oral microbiota and shifts systemic antibody parameters. PCOS and chronic periodontitis are associated with increased blood levels of oxidative products and reduced antioxidant status when oxidative stress circumstances are considered. Several papers have shown that there is a strong relationship between the risk factor for PCOS and periodontal disease and that women with PCOS are more likely to get periodontitis.

Finally, estrogen is the main female sex hormone affecting the oral tissues. It counteracts other sex hormones such as progesterone. Estrogen and progesterone effects can be considered synergistic, meaning that when combined, they can produce effects that are greater or different from those of each hormone acting alone. In this way, they act together to regulate the

menstrual cycle, creating a balance between follicular development, ovulation, and preparation for possible pregnancy. Also, they act together to create an optimal environment for a successful pregnancy. Estrogen promotes uterine growth and supports placental function, while progesterone maintains the uterine lining and prevents premature contractions, both of which are necessary for the pregnancy to proceed smoothly. On the other hand, estrogen alone is effective in protecting bone density, but progesterone may enhance estrogen's protective effects on bones by helping maintain the balance between bone formation and resorption, reducing the risk of osteoporosis, particularly in postmenopausal women (Toffoletto *et al.*, 2014).

CONCLUSIONS

- There appear to be challenges peculiar to every stage of life for any given female patient.
- The dentist should have a good understanding and appreciation of the science that underpins hormonal changes in women, and how they affect periodontal disease. Every single patient is unique when it comes to the way they will be faced throughout their lives
- Improved healthcare quality can be facilitated by scientific communication among medical professionals and medical and dental education programs.
- The dentist should have a good understanding and grasp of the mechanism for hormonal interaction of female sexuality and periodontal disease.
- It's critical to inform patients about the effects of hormone fluctuations on their oral health and to emphasize the importance of maintaining good oral hygiene.
- Every patient is different when it comes to how they are managed throughout their lives.
- The patient's awareness of hormonal changes and how they impact the health of their mouth, as well as other oral care advice, should be given.
- What is the accepted mechanism of these impacts on oral health remains incompletely answered question?

RECOMMENDATIONS

Regular dental visits are essential for maintaining oral health at all stages. The dentist should possess solid knowledge and comprehension of the mechanisms behind the relationship between female hormone fluctuations and periodontal disease.

REFERENCES

Abaffy, T.; Lu, HY. and Matsunami, H. (2023): Sex steroid hormone synthesis, metabolism, and the effects on the mammalian olfactory system. Cell Tissue Res. 2023;391(1):19-42.

Abe, J.; Jafarpour, S.; Vu, MH.; O'Brien, D.; Boyd, NK. and Vogel, BN. (2023): Impact of endocrine dysregulation on disability and non-motor symptoms in pediatric-onset multiple sclerosis. Front Neurol. 2023; 14: 1304610.

Adam, M. and Wooton J. (2022): Menopause and oral health. Br Dent J. 2022; 233(3): 170.

Agrawal, AT.; Hande, A.; Reche, A. and Paul, P. (2022): Appraisal of saliva and its sensory perception in reproductive transitions of women: a review. Cureus. 2022;14(11): e31614.

Alanazi, H.; Zhang, Y.; Fatunbi, J.; Luu, T. and Kwak-Kim, J. (2024): The impact of reproductive hormones on T cell immunity; normal and assisted reproductive cycles. J Reprod Immunol. 2024; 165: 104295.

Balan, P.; Chong, YS.; Umashankar, S.; Swarup, S.; Loke, WM. and Lopez, V. (2018): Keystone species in pregnancy

gingivitis: a snapshot of oral microbiome during pregnancy and postpartum period. Front Microbiol. 2018 9; 9: 2360.

Beksinska, ME.; Kleinschmidt, I. and Smit, JA. (2018): Bone mineral density in midlife long-term users of hormonal contraception in South Africa: relationship with obesity and menopausal status. Womens Midlife Health. 2018; 4: 6.

Bianchi, S.; Nottola, SA.; Torge, D.; Palmerini, MG.; Necozione, S. and Macchiarelli, G. (2020): Association between female reproductive health and mancozeb: Systematic review of experimental models. International Journal of Environmental Research and Public Health. 2020; 17: 1-15.

Boyapati, R.; Cherukuri, SA.; Bodduru, R. and Kiranmaye, A. (2021): Influence of female sex hormones in different stages of women on periodontium. J Midlife Health. 2021; 12(4): 263-6.

Buendía-González, FO. and Legorreta-Herrera M. (2022): The similarities and differences between the effects of testosterone and dhea on the innate and adaptive immune response. Biomolecules. 2022; 12(12): 1768.

Cecoro, G.; Paoletta, M.; Annunziata, M.; Laino, L.; Nastri, L. and Gimigliano, F. (2021): The role of bone anabolic drugs in the management of periodontitis: a scoping review. Eur Cell Mater. 2021; 41: 316-31.

Chen, P.; Hong, F. and Yu X. (2022): Prevalence of periodontal disease in pregnancy: A systematic review and meta-analysis. J Dent. 2022; 125: 104253.

Ciesielska, A.; Kusiak, A.; Ossowska, A. and Grzybowska, ME. (2022): Changes in the oral cavity in menopausal women—A narrative review. International Journal of Environmental Research and Public Health. 2022; 19: 1-12.

Cornejo Ulloa, P.; Van Der Veen, M.H. and Krom, B.P. (2019): Review: Modulation of the oral microbiome by the host to promote ecological balance. Odontology. 2019;107(4), 437-48.

Dassatti, L.; Manicone, PF.; Iavarone, F.; Stefanelli, N.; Nicoletti, F. and Lazzareschi, I. et al. (2019): Proteomic evaluation of GCF in the development of pregnancy related periodontal disease: a pilot clinical study. Eur Rev Med Pharmacol Sci. 2019; 23(12): 5030-9.

Di Naro, E.; Loverro, M.; Converti, I.; Loverro, MT.; Ferrara, E. and Rapone, B. (2021): The effect of menopause hypoestrogenism on osteogenic differentiation of periodontal ligament cells (PDLC) and stem cells (PDLCs): A systematic review. Health. 2021; 925: 1-11

Forsyth, KS.; Jiwrajka, N.; Lovell, CD.; Toothacre, NE. and Anguera, MC. (2024): The conneXion between sex and immune responses. Nat Rev Immunol. 2024; 24(7): 487-502.

Guan, C.; Zahid, S.; Minhas, AS.; Ouyang, P.; Vaught, A. and Baker, VL. (2022): Polycystic ovary syndrome: a "risk-enhancing" factor for cardiovascular disease. Fertil Steril. 2022;117(5): 924-35.

Handajani, J.; Effendi, N. and Sosroseno, W. (2020): Correlation between salivary estrogen levels and oral epithelial cytokeratin 5 expression. F1000Res. 2020; 9: 186.

Hanssen, H. (2021): Sex hormones and cardiovascular health: differentiation of the vascular bed is a key piece of the puzzle. Eur J Prev Cardiol. 2021;28(14):1588-9.

Huang, L.; Yuan, Y.; Ramirez, C.; Zhao, Z.; Chen, L. and Griebel, T. (2024): A receptor for dual ligands governs plant immunity and hormone response and is targeted by a nematode effector. Proc Natl Acad Sci U S A. 2024;121(42): e2412016121.

Huang, Z.; DerGarabedian, BP.; He, L.; Sha, Y.; Chen, Z. Kang, J. (2020): Impact of periodonto-pathogenic microbiota and sociodemographic variables on

periodontal status during pregnancy and postpartum period. Oral Health Prev Dent. 2020; 18:855-864.

Hutomo, DI.; Masulili, SLC.; Tadjoedin, FM, Kusdhany, LS. (2021): Serum alkaline phosphatase and calcium in relation to periodontal status among perimenopausal and postmenopausal women. The Open Dentistry Journal. 2021;15(1):703-8.

Iwobi, N. and Sparks, NR. (2023): Endocrine disruptor-induced bone damage due to hormone dysregulation: a review. Int J Mol Sci. 2023; 24(9): 8263.

Jafri, Z.; Bhardwaj, A.; Sawai, M. and Sultan, N. (2015): Influence of female sex hormones on periodontium: A case series. Journal of National Science and Biology Medicine. 2015; 6(1): S146-9.

Jayusman, PA.; Nasruddin, NS.; Baharin, B.; Ibrahim, N'.; Ahmad Hairi, H. and Shuid, AN. (2023): Overview on postmenopausal osteoporosis and periodontitis: The therapeutic potential of phytoestrogens against alveolar bone loss. Front Pharmacol. 2023 23; 14: 1120457.

Johnstone, C.; Hendry, C.; Farley A. and McLafferty, E. (2014): Endocrine system: part 1. Nurs Stand. 2014; 28(38): 42-9.

Kim, NY.; Kim, JE.; Choi, CH. and Chung, KH. (2024): Chronic kidney disease in postmenopausal women is associated with tooth loss. Menopause. 2024 1;31(8):663-8.

Kim, SM.; Shin, W.; Kim, HJ, Lee, JS.; Min, YK. and Yoon, BK. (2022): Effects of Combination oral contraceptives on bone mineral density and metabolism in perimenopausal korean women. J Menopausal Med. 2022; 28(1): 25-32.

Leucuta, DC.; Anton, D. and Almasan, O. (2024): Estrogen hormones' implications on the physiopathology of temporomandibular dysfunction. J Clin Med. 2024; 13(15): 4406.

Manos, J.T. (2022): he human microbiome in disease and pathology. APMIS. 2022; 130(12): 690-705.

Mary, KM. and Cherian, B. (2020): Evaluation of oral stereognosis, masticatory efficiency, and salivary flow rate in complete denture wearers. J Indian Prosthodont Soc. 2020; 20(3): 290-6.

Nastri, L.; Moretti, A.; Migliaccio, S.; Paoletta, M.; Annunziata, M. and Liguori, S. (2020): Do dietary supplements and nutraceuticals have effects on dental implant osseointegration? A scoping review. Nutrients. 2020; 12:1-16.

Niramitchainon, C.; Mongkornkarn, S.; Sritara, C.; Lertpimonchai, A. and Udomsak, A. (2020): Trabecular bone score, a new bone quality index, is associated with severe periodontitis. J Periodontol. 2020; 91: 1264–73.

Ozgen Ozturk, V.; Meriç, P.; Sorsa, T.; Tervahartiala, T. and Bostanci, N. (2021): Regulation of matrix metalloproteinases-8, -9 and endogenous tissue inhibitor-1 in oral biofluids during pregnancy and postpartum. Arch Oral Biol. 2021; 124: 105065.

Park, CO.; Lee, SE.; Yoon, JW.; Park, HJ.; Kim, SH. and Oh, SH. (2022): Comparison of three antioxidants in chemical and biological assays on porcine oocytes during ageing in vitro. Zygote. 2022; 30(4) 561-70.

Penoni, DC.; Fidalgo, TK; Torres, SR.; Varela, VM.; Masterson, D. and Leão, AT. (2017): Bone density and clinical periodontal attachment in postmenopausal women: a systematic review and meta-analysis. J Dent Res. 2017; 96(3): 261-9.

Pompili, A.; Iorio, C. and Gasbarri, A. (2020): Effects of sex steroid hormones on memory. Acta Neurobiol Exp (Wars). 2020; 80(2):117-28.

Prachi, S.; Jitender, S.; Rahul, C.; Jitendra, K.; Priyanka, M. and Disha, S. (2019): Impact of oral contraceptives on periodontal health. Afr Health Sci. 2019;19(1):1795-1800.

Qi, J.; Chen, J.; Pang, Y.; Guo, Y.; Chen, G. and Liu Y. (2023): Association between periodontal disease and osteoporosis in postmenopausal women: A systematic review and meta-analysis. Heliyon. 2023; 9(11): e20922.

Rogowska, AM.; Tataruch, R. and Klimowska, K. (2023): Validation of the shortened 24-item multidimensional assessment of interoceptive awareness, version 2 (Brief MAIA-2). Sci Rep. 2023; 13(1): 21270.

Rojo, MG. and Lloret, MRP. (2024): Gironés, JG. Oral manifestations in women using hormonal contraceptive methods: a systematic review. Clin Oral Investig. 2024; 28(3): 184.

Rukmini, JN.; Sachan, R.; Sibi, N.; Meghana, A. and Malar, CI. (2018): Effect of menopause on saliva and dental health. Journal of International Society. 2018; 8: 529-33.

Saadaoui, M.; Singh, P. and Al Khodor, S. (2021): Oral microbiome and pregnancy: A bidirectional relationship. J Reprod Immunol. 2021; 145: 103293.

Sanfilippo, JS. and Lara-Torre, E. (2009): Adolescent gynecology. Obstet Gynecol. 2009;113(4): 935-47.

Sathish, AK.; Varghese, J. and Fernandes, AJ. (2022): The Impact of Sex Hormones on the Periodontium During a Woman's Lifetime: a Concise-Review Update. Curr Oral Health Rep. 2022; 9: 146-56.

Savić Pavičin, I.; Dumančić, J.; Jukić, T. and Badel, T. (2017): The relationship between periodontal disease, tooth loss and decreased skeletal bone mineral density in ageing women. Gerodontology. 2017; 34: 441–5.

Sumadhura, C.; Prasanna, JS. and Sindhura, C. and Karunakar, P. (2018): Evaluation of periodontal response to nonsurgical therapy in pre- and post-menopausal women with periodontitis. Indian J Dent Res. 2018; 29(3): 298-302.

Sumbayak, IA.; Masulili, SLC.; Tadjoedin, FM.; Sulijaya, B.; Mutiara, A. and Khoirowati, D. (2023): Changes in interleukin-1beta, tumor necrosis factor-alpha, and interleukin-10 cytokines in older people with periodontitis. Geriatrics (Basel). 2023; 8(4): 79.

Sumit, K.; Vikram, K.; Rajlaxmi, M.; Ranjitkumar, P.; Anastasios, G. and Abhishek K. (2024): Evaluation of oral health, taste perception, nutritional status and emotional well-being in post-menopausal women. J Oral Rehabil. 2024; 51(9): 1833-8.

Tarkowská, D. (2019): Plants are capable of synthesizing animal steroid hormones. Molecules. 2019; 24(14): 2585.

Thomas, MP. and Potter, BV. (2013): The structural biology of oestrogen metabolism. J Steroid Biochem Mol Biol. 2013; 137: 27-49.

Toffoletto, S.; Lanzenberger, R.; Gingnell, M. and Sundström-Poromaa I. (2014): Comasco Emotional and cognitive functional imaging of estrogen and progesterone effects in the female human brain: a systematic review. E. Psychoneuroendocrinology. 2014; 50:28-52.

Van Den Beld, AW.; Kaufman, JM.; Zillikens, MC.; Lamberts, SWJ.; Egan, JM. and Van Der Lely, AJ. (2018): The physiology of endocrine systems with ageing. Lancet Diabetes Endocrinol. 2018; 6(8): 647-58.

Villalobos, V.; Garrido, M.; Reyes, A.; Fernández, C.; Diaz, C. and Torres, VA. (2022): Aging envisage imbalance of the periodontium: A keystone in oral disease and systemic health. Front Immunol. 2022; 13: 1044334.

Wang, Y. and Kinoshita, T. (2023): The role of lipid scramblases in regulating lipid distributions at cellular membranes. Biochem Soc Trans. 2023; 51(5): 1857-69.

Yakar, N.; Bostanci, N.; Özdemir, G.; Atmaca, H.; Türedi, A. and Şahin, Ç. (2024): Salivary inflammatory burden

in pre- and postmenopausal women: Associations with body mass index, patient-reported health, serum cytokines, and periodontal parameters. J Periodontol. 2024; 95(3): 209-18.

Yakar, N.; Türedi, A.; Emingil, G.; Şahin, Ç.; Köse, T. and Silbereisen, A. (2021): Oral health and emotional well-being in premenopausal and postmenopausal women: a cross-sectional cohort study. BMC Womens Health. 2021; 21(1): 338.

Yang, X.; Tian, Y.; Zheng, L.; Luu, T. and Kwak-Kim, J. (2022): The update immune-regulatory role of pro- and anti-inflammatory cytokines in recurrent pregnancy losses. Int J Mol Sci. 2022; 24(1): 132.

دور هرمون الإستروجين في سلامة أنسجة الفم

عاطف أسماعيل أحمد، فراس دحيل السليحات، محمود عبدالسلام عطية، أحمد محمد حسين

Email: ahmedattay@dent.aun.edu.eg Assiut University web-site: www.aun.edu.eg

تعكس وظائف أنسجة الفم المختلفة الحالة الصحية العامة للإفراد. العديد من الهرمونات الجنسية لها تأثيرات فعاله علي أنسجة الفم كما يعتقد أنها تمتلك بعض الخصائص العلاجية. وقد استهدفت العديد من الدراسات آثار تقلبات تلك الهرمونات على الأنسجة المختلفة للفم، وخاصة أنسجة اللثة. هناك العديد من التغييرات التي تحدث نتيجة لنقص هرمون الاستروجين من بينها التغيرات علي الأنسجة الفموية. تشمل التغييرات: انخفاض إفراز اللعاب وزيادة قابلية الغشاء المخاطي المبطن للفم للتقرح وكذلك قد يؤدي إلي جفاف أنسجة الفم وزيادة تسوس الأسنان. بالإضافة إلى أن انخفاض اللعاب يؤثر علي صحة أنسجة اللثة وبالتالي قد يؤدي ذلك إلى زيادة خلخلة الأسنان وربما فقدان الأسنان بسبب زيادة البكتيريا في الأنسجة المحيطة للأسنان. نظرًا لأن مرض اللثة هو أحد الأشياء التي تقلل من جودة الحالة الصحية للأفراد، فإن الوقاية من هذا الضرر وعلاجه أمر ضروري. ولتحديد الدراسات التي تعالج هذا الموضوع، فإن السؤال الرئيسي الذي تم البحث عنه هو: "هل هناك أي علاقة بين تركيز هرمون الإستروجين في سوائل الجسم وسلامة الأنسجة الفموية وحالتها الصحية؟". وقد كشفت هذه المراجعة أن توازن هرمون الإستروجين في الجسم مع أنسجة اللثة ثابت. وكان هدف البحث هو تحديد ما إذا كانت صحة الأنسجة الفموية مرتبطة بالهرمونات الجنسية. بحيث يتمتع طبيب الأسنان بفهم جيد للتغيرات الهرمونية لدى النساء، وكيف تؤثر على أمراض اللثة.