**Republic of Iraq**
**Ministry of Higher Education and Scientific Research University of Alzahrawi College of Dentistry**

# Effect of hormonal changes on periodontal health in pregnant women (comparative study)

A thesis
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By

Ahmed Adnan Abd Al-Hussein
Ayah Abbas Fadel
Mariam Najeh Nouri
Rawan Majed Hadi

Supervised by
**Dr. Asma Mohammed Mahna**
**B.D.S., M.Sc.**

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# DEDICATION

To my first and last supporter, my beloved, my heaven, mama.

To my dear father for his support and encouragement to reach my dream.

# ACKNOWLEDGMENTS

My great and deep thanks to **Allah almighty** for giving me this opportunity and the strength to complete our project.

Sincere thanks and respect to**,**

# ABSTRACT

**Introduction:**

**Subjects, Materials and Methods:**

**Results:**

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# LIST OF ABBREVIATIONS AND SYMBOL

| | |
|---|---|
| **%** | Percentage |
| **1st** | First |
| **2nd** | Second |
| **3rd** | Third |
| **ADA** | American Dental Association |
| **ANOVA** | Analysis of Variance |
| **BMD** | Bone mineral density |
| **Ca** | Calcium |
| **CAL** | Clinical attachment loss |
| **CEQ** | Closed end question |
| **CPI** | Community periodontal index |
| **D.W** | Distilled water |
| **DMFS** | Decay, missed, filled surface index |
| **DMFT** | Decay, missed, filled teeth index |
| **DS** | Decayed surface |
| **DT** | Decayed teeth |
| **ELISA** | Enzyme linked immunosorbent assay |
| **FDI** | Federation Dentaire Internationale |
| **Fl** | Flerovium |
| **FS** | Filled surface |
| **FT** | Filled teeth |
| **GI** | Gingival index |
| **$H_2O$** | Water |
| **HCl** | Hydrochloric acid |
| **HPR** | Horse Radish Perioxidase |
| **ICC** | Intraclass correlation coefficient |
| **IU** | International unit |
| **KAB** | Knowledge, attitude and behavior |
| **$LaCl_3$** | Lanthanum chloride |
| **MCQ** | Multiple choice question |
| **mL** | Milliliter |
| **mmol/L** | millimol/liter |
| **MS** | Missing surface |
| **MT** | Missing teeth |

| | |
|---|---|
| **N** | Number |
| **Ng/ml** | Nanogram per millileter |
| **nm** | Nanometer |
| **OD** | Optical density |
| **P** | Phosphors ion |
| **p. value** | Probability value |
| **PD** | Periodontal disease |
| **PDD** | Periodontal pocket depth |
| **pH** | Potential of hydrogen |
| **PlI** | Plaque index |
| **$PO_4$** | Phosphate |
| **ppm** | Part per million |
| **r factor** | Pearson correlation |
| **rs** | Sperman correlation |
| **rpm** | Revolution per minute |
| **SD** | Standard deviation |
| **SE** | Standard error |
| **SPSS** | Statistical Package for Social Sciences |
| **T-test** | T- sample test |
| **TTW** | Total tooth wear |
| **US foods** | United signature foods |
| **VD3** | Vitamin D3 |
| **WHO** | World health organization |
| **W/V** | Weight /volume |
| **µL** | Microliter |

# INTRODUCTION

Pregnancy is a unique physiological state characterized by significant hormonal and immunological changes that profoundly impact a woman's health. Among the various health aspects affected, oral health has gained attention, as the alterations that occur during pregnancy can increase susceptibility to oral diseases such as periodontal disease and dental caries. The immune system adaptations during this period can diminish the body's capacity to respond effectively to oral infections, complicating the maintenance of oral health.. ( Srinivas S et al, 2012).

Research indicates that the interplay between physiological and hormonal changes during pregnancy can lead to heightened vulnerability to periodontal diseases, which are among the most prevalent health issues faced by pregnant women. Despite the increasing awareness of oral health during pregnancy, findings from studies investigating the relationship between pregnancy and oral health remain inconclusive. Factors such as dental plaque accumulation, microbial composition variations, salivary changes, and pH decreases are believed to contribute to the frequent occurrence of these oral diseases during pregnancy..(Fatma Y et al ,2024).

Bacterial plaque is the main cause of periodontal disease initiation. Additionally, sex hormones play a significant role as modifying factors that affect the development of these diseases. Although extensive research has established a connection between periodontal health and the dynamics of sex hormones, the precise molecular mechanisms and therapeutic approaches are still not fully understood. Fatma Y et al ,2024).

periodontal disease is one component of oral health that is linked to pregnancy. Periodontal disorders are frequent chronic inflammatory illnesses with multiple etiologies; nonetheless, gingivitis is the most common kind of periodontal disease encountered in pregnancy (Chickanna et al., 2015). The increased secretion of gestational hormones (especially estrogen and progesterone) during pregnancy has been linked to pregnancy gingivitis (Yalcin et al., 2002; Gursoy et al., 2008; Ortiz-Sanchez et al., 2021). Iraqi studies have been conducted the severity of gingivitis in pregnant women a controversy results were recorded (Mohammed, 2005; AL-Zaidi, 2007; Issa, 2011; Mutlak, 2016; Al Najjar, 2018; Baydaa Hussein, 2019).

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# AIM OF THE STUDY

**Aim**: to investigate the impact of hormonal changes during pregnancy on periodontal health in pregnant women

# CHAPTER ONE
# REVIEW OF LITERATURE

# REVIEW OF LITERATURE

## 1. Periodontal diseases

### 1.1. Definition

Periodontal diseases are inflammatory conditions that impact the supporting structures of the teeth, including the gums, periodontal ligament, cementum, and alveolar bone. These diseases arise from the interaction between bacteria and the immune response of the host. The presence of harmful microorganisms plays a crucial role in the development and progression of periodontal diseases, and how the body responds to these pathogens is also significant in the advancement of the disease. **(Craig, 2003).**

Periodontal diseases are classified into gingivitis and periodontitis. Gingivitis may be defined as the gingival inflammation; It is reversible with good oral hygiene practice by the patient him or herself **(Armitage, 2004).**

While periodontitis is the more destructive form of periodontal diseases, In which the inflammation extends to the alveolar bone that support the teeth and results in periodontal pocket formation, periodontium destruction, attachment loss, alveolar bone resorption, and these symptoms will lead to tooth mobility and finally tooth loss **(Carranza, 2012).**

Several risk factors contribute to the increase of periodontal disease, including cigarette smoking, systemic illnesses, certain medications like steroids, anti-epileptic drugs, and cancer treatment drugs. Other contributing factors include ill-fitting dental bridges, misaligned teeth, and loose fillings, as well as pregnancy and the use of oral contraceptives. Additionally, any medical condition that affects the body's antibacterial defense mechanisms, such as human immunodeficiency virus (HIV) infection, diabetes, and disorders related to neutrophils, is likely to exacerbate periodontal disease. **(Loesche and Grossman, 2001).**

When evaluating the severity of periodontal disease, probing depth serves as an effective measure of disease progression. In a healthy periodontal condition, there are no losses of epithelial attachment or formation of pockets, and the depth of the gingival sulcus typically ranges from 2 to 3 mm. **(Angeli *et al.*, 2003).**

Periodontal pockets can extend between 4 and 12 mm. clinically, patients with periodontal pockets of 4 mm or more are diagnosed with periodontitis. Patients with periodontal pockets of 6 mm or more are diagnosed with advanced or severe periodontitis **(Elter *et al.*, 2004).**

## classification of periodontal diseases

The classification of periodontal diseases established by the American Academy of Periodontology (AAP) and the European Federation of Periodontology (EFP) in 2018 is outlined as follows:

Periodontal Health, Gingival Diseases, and Conditions

1. Periodontal health and gingival health
   - a) Clinical gingival health on an intact periodontium
   - b) Clinical gingival health on a reduced periodontium
2. Gingivitis: Dental Biofilm Induced
   - a) Associated with dental biofilm alone
   - b) Mediated by systemic or local risk factors
   - c) Drug-influenced gingival enlargement
3. Gingival Diseases: Non-Dental Biofilm-Induced

Periodontitis

1. Necrotizing periodontal diseases
2. Periodontitis
3. Periodontitis as Manifestation of Systemic Diseases

Systemic and Other Periodontal Conditions

1. Systemic diseases or conditions affecting the periodontal supporting tissues
2. Other Periodontal Conditions



3. Mucogingival Deformities and Conditions around teeth

4. Traumatic Occlusal Forces
5. Prosthesis and tooth-related factors that modify or predispose to plaque-induced diseases/periodontitis

Peri-implant Diseases and Conditions

1. Peri-implant health
2. Peri-implant mucositis
3. Peri-implantitis
4. Peri-implant soft and hard tissue deficiencies

# Gingivitis

Plaque-induced gingivitis is the most prevalent type of periodontal disease (Califano, 2003) and is recognized as the second most common oral condition after dental caries, impacting over 75% of people globally. **(Petersen 2003, Papapanou 1999).**

Gingivitis is commonly recognized as a localized inflammatory condition triggered by the buildup of dental biofilm (Holmstrup et al., 2018). It is marked by symptoms such as gum bleeding, redness, and swelling, without any loss of periodontal attachment (Murakami et al., 2018). The ongoing nature of this inflammation is associated with the presence of microbial dental plaque. The inflammation will persist as long as this microbial biofilm remains near the gum tissues. **(Silness, 1964)**, figure (1-1).

When compared to periodontitis, a peculiarity of plaque-induced gingivitis is the complete reversibility of the tissue alterations once the dental biofilm is removed. Notwithstanding the reversibility of the gingivitis-elicited tissue changes, gingivitis

holds particular clinical significance because it is considered the precursor of periodontitis, a disease characterized by gingival inflammation combined with connective tissue attachment and bone loss **(Trombelli *et al.*, 2018).**

Figure (1-1): Plaque induced gingivitis **(Bathla, 2017).**

## Chronic Periodontitis

Chronic periodontitis is an inflammatory disease that arises from multiple factors, linked to imbalanced dental plaque biofilms, and is marked by the gradual destruction of the structures that support the teeth (Papapanou, 2017). It poses a significant public health challenge due to its widespread occurrence and potential to result in tooth loss and impairment. Additionally, chronic periodontitis adversely impacts chewing ability, which can, in turn, affect nutrition; it also contributes to social inequalities and diminishes overall quality of life. **(Kassebaum, 2014)**, figure (1- 2).

Cases of periodontitis are assessed through various clinical parameters, which include clinical attachment level (CAL), probing depth (PD), bleeding on probing (BoP), and the extent of radiographic bone loss. **(Palmer *et al.*, 1999).**

The severity of periodontitis is evaluated according to the degree of attachment loss: 1-2 mm is regarded as mild, 3-4 mm as moderate, and 5 mm or more as severe periodontitis. The distinction between aggressive and chronic periodontitis is not clearly defined and relies on clinical characteristics. **(Bunæs, 2017).**



In contrast to aggressive periodontitis, chronic periodontitis lesions are typically found in adults without any particular familial pattern. This condition is marked by a persistent deterioration of periodontal tissues linked to subgingival plaque, calculus, and various individual risk factors. **(Shchipkova et al., 2010).**

The progression of chronic periodontitis seems to be continuous with slow to moderate bursts of tissue destruction slowing off later in life **(Bagaitkar *et al.*, 2011).**

The removal of calculus, management of plaque, and control of gingivitis are crucial in preventing the advancement of chronic periodontitis, further attachment loss, and eventual tooth loss. **(Ramseier *et al.*, 2017).**

Figure (1- 2): **Chronic periodontitis**

## 1. Pregnancy

Pregnancy is typically a physiological process that affects women and can result in a variety of physical, psychological, and hormonal changes (Soulissa, 2014).

The average duration of pregnancy is approximately 40 weeks, calculated from the first day of the last menstrual period (LMP), and is divided into three trimesters. The first trimester spans from week one to week twelve and encompasses conception, which occurs when a sperm fertilizes an egg. The resulting zygote then moves down the fallopian tube and implants itself in the uterus, where it begins developing into a fetus and placenta. The second trimester lasts from week thirteen to week twentyeight, during which the fetus's movements may be felt around the midpoint. The third trimester extends from week twenty-nine to week forty. (Wiliams and Wilkins, 2012).

During pregnancy, the mother's body undergoes physiological changes designed to support the growth and homeostasis of the fetus while safeguarding her own health. These adjustments occur in the circulatory, respiratory, renal, and endocrine systems, ensuring that the fetus receives necessary energy and nutrients while efficiently removing excess heat and waste products. (Hacker et al., 2015).

## 2. Systemic changes during pregnancy

### ❖ Changes in the body weight

Ongoing weight gain during pregnancy is seen as a positive sign of the mother's adaptation and the baby's growth. This weight gain is associated with the baby's weight, the placenta, additional circulatory fluid, increased tissue mass, and reserves of fat and protein. (Lammi-Keefe et al., 2008).

### ❖ Morning sickness

Morning sickness, characterized by nausea and vomiting during pregnancy (NVP), affects up to 80% of pregnancies globally (Chortatos et al., 2013). Although it can occur at any time, it is most prevalent in the morning. Various theories suggest its causes, including infections, hormonal changes, and vitamin deficiencies (Jennifer and Niebyl, 2010). Typically, nausea symptoms subside by the 20th week, but around 10–20% of individuals may continue to experience them beyond this point, with some enduring symptoms until the end of their pregnancy. (Clark et al., 2012).

Hyperemesis gravidarum (HG) are characterised by severe nausea and vomiting. This is seen in 1-3% of women presenting with NVP and can lead to hospitalisation, malnutrition, weight loss, vitamin deficiencies and low birth weights (Clark et al., 2012).

### ❖ Cardiac and blood changes

During pregnancy, total blood volume increases by approximately 40% compared to pre-pregnancy levels, with considerable individual variation. Plasma volume begins to rise as early as the sixth week and levels off around 32 to 34 weeks, after which changes are minimal. In the second trimester, red blood cell mass starts to increase and continues to do so until delivery, reaching levels 20-35% higher than in non-pregnant individuals. This increase in plasma volume relative to red cell volume leads to hemodilution, often described as the physiological anemia of pregnancy, which results in lower hematocrit values.

By the tenth week, cardiac output has grown about 40% above non-pregnant levels, stabilizing from 20 to 24 weeks onward. This increase in cardiac output is due primarily to a rise in stroke volume (10-30%) during the first and second trimesters, while heart rate also increases slightly (by 12-18 beats per minute). Cardiac output peaks as blood volume continues to rise. Systolic blood pressure experiences a minor drop of 4-6 mm Hg, while diastolic pressure decreases more significantly by 8-15 mm Hg. This decline begins in the first trimester, reaches its lowest point in mid-pregnancy, and gradually returns toward non-pregnant levels by the end of pregnancy. These physiological changes are indicative of increased cardiac output and decreased peripheral resistance characteristic of pregnancy. (Hacker et al., 2015).

- **Renal system changes**

During pregnancy, renal plasma flow and glomerular filtration rate (GFR) increase significantly, with rises of 40–65% and 50–85%, respectively, compared to non-pregnant levels. Additionally, the increase in plasma volume leads to a reduction in oncotic pressure within the glomeruli, which further contributes to the rise in GFR. (Cheung and Lafayette, 2013).

Vascular resistance decreases in both the afferent and efferent arterioles of the kidneys, allowing glomerular hydrostatic pressure to remain stable despite the significant increase in renal plasma flow, thus preventing glomerular hypertension (Priya et al., 2016). Additionally, the heightened renal blood flow during pregnancy leads to an increase in renal size by 1–1.5 cm, reaching its peak by mid-pregnancy. The mechanical pressures exerted on the ureters result in the dilation of the kidney, pelvis, and calyceal systems. These structural changes are influenced by progesterone, which decreases ureteral tone, peristalsis, and contraction pressure. (Cheung and Lafayette, 2013).

## 3. Ovarian changes

Estrogens and progestin are ovarian sex hormones primarily synthesized from cholesterol derived from the bloodstream, with a smaller contribution from acetyl coenzyme A, in the ovaries (Hall, 2015). The synthesis of these hormones begins with the anterior pituitary gland, which releases gonadotropins, specifically follicle stimulating hormone (FSH) and luteinizing hormone (LH), after receiving signals from hypothalamic gonadotropin-releasing hormone (GnRH). In turn, FSH and LH stimulate the production of estrogens and progestin. (Boron and Boulpaep, 2012).

### 3.1. Estrogen

Estrogen, also referred to as oestrogen, is a female sex hormone that facilitates the growth and division of specific cells in the body that contribute to the development of secondary sexual characteristics in females. Additionally, human female plasma contains significant levels of three primary estrogens: estradiol, estrone, and estriol. Another form of estrogen, estetrol (E4), is uniquely produced during pregnancy. (Hall, 2015).

Estrogen daily production from placenta during the pregnancy increases times from normal range (25-75 pg/ml) toward the end of the pregnancy. During pregnancy, main functions of estrogen include (Hall, 2015):

- Enlargement of the uterus of mother.
- Enlargement of the mother's breasts and growth of the breast ductal structure.Enlargement of the mother's female external genitalia. The estrogens also relax the pelvic ligaments of the mother, so the sacroiliac joints become relatively limber and the symphysis pubis becomes elastic.
- These changes allow easier passage of the fetus through the birth canal.There is much reason to believe that estrogens also affect many general aspects of fetal development during pregnancy, for example, by affecting the rate of cell reproduction in the early embryo (Hall, 2015).

### 3.2. Progesterone

Progesterone is a steroid with 21 carbon atoms that acts as a precursor in the synthesis of other steroids. It is predominantly produced by the granulosa-lutein cells in the corpus luteum (CL) during the luteal phase of the menstrual cycle (Niswender et al., 2000). Progesterone has two primary functions: it induces secretory changes in the uterine endometrium during the latter part of the menstrual cycle, preparing the uterus for the implantation of a fertilized egg, and it decreases the frequency and intensity of uterine contractions, helping to prevent the expulsion of the implanted egg. Progesterone is equally important as estrogen for a healthy pregnancy. Initially, the corpus luteum secretes moderate amounts of progesterone at the beginning of pregnancy, but later on, the placenta produces it in larger quantities. The following unique effects of progesterone are crucial for the proper advancement of pregnancy. (Hall, 2015):

- Progesterone causes decidual cells to develop in the uterine endometrium.These cells play an important role in the nutrition of the early embryo.
- Progesterone decreases the contractility of the pregnant uterus, thus preventing uterine contractions from causing spontaneous abortion.

- Progesterone contributes to the development of the conceptus even before implantation because it specifically increases the secretions of the mother's fallopian tubes and uterus to provide appropriate nutritive matter for the developing morula (the spherical mass of 16 to 32 blastomeres formed before the blastula) and blastocyst. There is also reason to believe that progesterone affects cell cleavage in the early developing embryo.
- The progesterone secreted during pregnancy helps estrogen in preparing the mother's breasts for lactation.

## 4. Oral hygiene and oral health status among pregnant women.

Oral health is vital for overall well-being but is often neglected by women during pregnancy, especially those from low-income backgrounds (Wagner and Heinrich-Weltzien, 2016). Pregnancy is a challenging condition that brings about considerable changes in metabolic and physiological functions (Soulissa, 2014). Consequently, some of the most significant physiological and hormonal transformations in a woman's life occur during this period (Laine, 2002), with particular emphasis on the oral cavity (Marla et al., 2018). These changes can manifest as pregnancy gingivitis, benign oral lesions, tooth mobility, tooth erosion, cavities, and periodontitis. (Amar and Chung, 2000; Annan and Nuamah, 2005; AL-Sultani., 2013)

Research conducted by Massoni et al. and Ho and Chou indicates that hormonal fluctuations during pregnancy influence the amount of biofilm present in periodontal tissues. For pregnant women, there is a positive correlation between the total subgingival bacteria and the severity of clinical diagnoses. Specifically, **Porphyromonas gingivalis** is known to thrive during the first trimester, as it utilizes progesterone as a growth factor in place of vitamin K. Additionally, the levels of various bacteria in the periodontal tissues—such as **Prevotella intermedia**, **Bacteroides melaninogenicus** ss., and **Fusobacterium nucleatum**—also correlate positively with hormone concentrations

Fluctuations in sex steroid hormones throughout pregnancy can significantly impact the metabolism of periodontal tissue. According to findings from González-Jaranay et al., Edize et al., and Vidhale et al., most pregnant women experience gingivitis and periodontitis during all trimesters, with these conditions being particularly more common and severe during the third trimester compared to earlier stages of pregnancy and after delivery. Symptoms of gingivitis typically arise in the second month of pregnancy and worsen until the eighth month, followed by a regression postpartum that aligns with hormone concentration changes.

Periodontal tissue is notably affected by estrogen and progesterone, as increased levels of these hormones can stimulate human gingival fibroblasts to produce a higher quantity of cytokines. Pro-inflammatory cytokines like interleukin-6 (IL-6) and IL-8 can trigger and amplify inflammatory processes within the tissues. An increase in cytokine production has been linked to periodontal tissue damage, as it may interfere with neutrophil function—an important anti-inflammatory mechanism—and lead to an exaggerated inflammatory response to oral infections.

Elevated levels of estrogen and progesterone result in increased vascular permeability and capillary dilation in the gingival tissues, making them more susceptible to inflammation. Estrogen specifically enhances vascular permeability by altering the endothelial cells that line blood vessels, leading to fluid retention in gingival tissues and raising the risk of inflammation and bleeding. This heightened vascular response significantly contributes to pregnancy gingivitis, which affects 60–70% of pregnant individuals.

Additionally, hormonal changes during pregnancy affect the immune system, leading to an altered immune response in gingival tissues. Progesterone can weaken local immune defenses by diminishing the effectiveness of neutrophils and macrophages against bacterial plaque. This immunosuppressive effect facilitates bacterial buildup and gingival inflammation, thereby increasing the risk of periodontal disease progression during pregnancy.

## Pregnancy Gingivitis

In 1877, Pinard documented the first instance of "pregnancy gingivitis." Epidemiological studies have shown its prevalence varying from 35% (Hasson 1966) to 100% (Lundgren et al. 1973). This condition is characterized by redness, swelling, overgrowth of gum tissue, and increased bleeding, with a histological profile similar to gingivitis. The front part of the mouth is more frequently affected, and interproximal areas are often involved (De Liefde 1984).

The heightened tissue swelling leads to deeper pockets and can cause temporary tooth mobility. Inflammation in the anterior region may worsen due to increased mouth breathing resulting from pregnancy rhinitis. A study by Machuca et al. (1999) on 130 pregnant women found gingivitis present in 68% of participants, ranging from 46% among technical executives to 88% among manual workers. Cross-sectional studies comparing pregnant and postpartum women indicate that pregnancy is linked to significantly higher rates of gingivitis, even with similar plaque scores (Silness & Loe 1963).

A more recent investigation involving a rural population of Sri Lankan women (Tilakaratne et al. 2000) revealed varying degrees of increased gingivitis among pregnant women compared to non-pregnant controls. The study showed a progressive rise in inflammation as pregnancy advanced, particularly notable in the second and third trimesters, despite plaque levels remaining steady. Three months after delivery, the level of gingival inflammation was comparable to what was observed in the first trimester of pregnancy. This indicates a direct relationship between gingivitis and sustained elevated levels of gestational hormones during pregnancy, with a decrease during the postpartum period. Investigations by Cohen et al. (1969) and Tilakaratne et al. (2000) found that the levels of attachment loss remained unchanged throughout pregnancy and three months after childbirth.

## pregnancy tumor

A pregnancy tumor is a pedunculated or sessile fibro-granulomatous growth that sometimes emerges during pregnancy. Its development is influenced by the vascular response triggered by progesterone along with the matrix-stimulating effects of estradiol, typically at locations where gingivitis already exists. These lesions commonly appear on the anterior papillae of the maxillary teeth and generally do not exceed 2 cm in diameter. They can bleed if injured, and it is advisable to postpone their removal until after childbirth, as significant reduction in size often occurs post-delivery (Wang et al. 1997). Attempting surgical excision of the granuloma during pregnancy may lead to recurrence due to inadequate plaque control and hormone-related growth of the lesion. Maintaining diligent oral hygiene and performing debridement during pregnancy is crucial to help prevent the formation of these tumors (Wang et al. 1997).

- **Calcium and its relation to oral health status during pregnancy**

Saliva contains a considerable amount of calcium, and any variations in its levels can affect dental and oral health (Bakhshi et al., 2012). Total calcium levels in both stimulated and unstimulated saliva are typically lower during pregnancy compared to non-pregnant women (Öztürk et al., 2013). However, research indicates no significant differences in the total calcium content of saliva between pregnant and non-pregnant women (Guidozzi et al., 1992; Salvolini et al., 1998; Rockenbach et al., 2006). Calcium concentrations in saliva generally range from 1-3 mmol/L, influenced by salivary flow rates. When saliva shifts from an unstimulated to a stimulated state, the calcium concentration tends to drop. Given that calcium levels in submandibular and sublingual saliva are approximately twice that found in parotid saliva, this reduction during stimulation may result from an increase in the secretion of saliva from the parotid glands (Khan et al., 2005; Preethi et al., 2010).

Calcium in saliva exists in two forms: ionized forms, which are essential for processes related to dental caries, and bound forms, such as calcium phosphate, which depend on the pH of the saliva. Ionized calcium makes up 50% of the total calcium concentration at average pH levels but increases as the salivary pH decreases; below a pH of 4, a significant portion of salivary calcium becomes ionized (Tibor et al., 2007; David, 2009; Preethi et al., 2010). Non-ionized calcium is associated with inorganic phosphate, bicarbonate, proteins (including prolin-rich protein, histidine, and statherin), organic acids (such as citric acid and uric acid), enzymes, and dietary carbohydrates (like monosaccharides, oligosaccharides, and polysaccharides). (David, 2009).



Calcium plays essential roles in saliva, including maintaining solubility products, supporting tooth structure, and activating enzymes (Choi, 2010). Enamel, primarily composed of hydroxyapatite (calcium and phosphate), benefits from saliva during the maturation process as teeth erupt and offers protection in the oral environment. The calcium ions in saliva help to stabilize hard dental tissues, so a reduction in their concentration during pregnancy may raise the risk of dental caries (Bakhshi et al., 2012). While it is commonly believed that calcium is depleted from a mother's teeth to support the developing fetus, research indicates that there is "no significant withdrawal of calcium or other minerals from the tooth." Instead, it is the surrounding environment of the teeth that is affected (Laine, 2002).

During pregnancy, changes in saliva composition and oral microbiome, along with factors like vomiting, dietary alterations, and inadequate oral hygiene, may contribute to increased caries risk (Vadiakas and Lianos, 1988). This underscores the importance of calcium, as its presence in saliva can significantly influence remineralization and enhance the acid resistance of the outer enamel surface (de Almeida et al., 2008). Research findings indicate that lower salivary calcium levels are linked to a higher incidence of dental caries (Kamate et al., 2017). Similar results have been observed in studies conducted in Iraq, revealing an inverse relationship between dental caries experience and calcium levels. ( Hasan and Diab, 2010; Aziz, 2014; Kadoum and Salih, 2014; Al-Tamimi and Al-Rawi, 2018; Al-Rawi, 2019).

According to Iraqi study conducted on pregnant women, it was found

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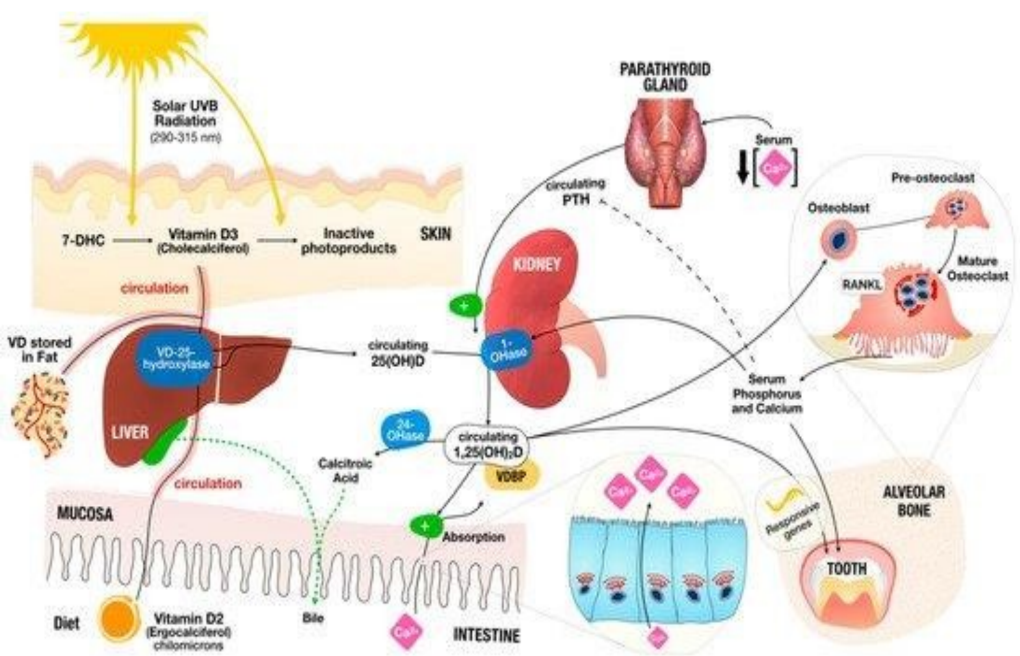

**Figure: (1-1) Metabolism of vitamin D3 in the body.**

Teeth are mineralized organs surrounded by alveolar bone and formed by enamel, dentin, and cementum, which are three distinct hard tissues. While tooth mineralization is similar to skeletal mineralization, if mineral metabolism is disrupted, failures similar to those seen in bone tissue will occur. Vitamin D is essential for bone and tooth mineralization, and when levels aren't controlled, it can result in the "rachitic tooth," a deficient and hypomineralized organ that's prone to fracture and decay (Foster et al., 2014; D'Ortenzio et al., 2018).

Vitamin D influences the pathogenesis of periodontal diseases (PD) by immunomodulation, raises bone mineral density (BMD), lowers bone resorption, and aids in the combat against periodontal disease-causing agents. There has been a surge of interest in and publication of studies on vitamin D's involvement in preventing and treating dental caries and periodontal disease (Schwalfenberg, 2011; Anand et al., 2013; Jagelavičienė et al., 2018). Researches has discovered links between periodontal health, Ca and vitamin D intake (Nishida et al., 2000; Dietrich et al.,2004) indicating that dietary calcium and vitamin D supplementation can enhance periodontal health, mandibular bone mineral density, and prevent alveolar bone loss (Hildebolt et al, 2004; Miley et al., 2009). Calcium and vitamin D supplementation at dosages greater than 800-1,000 IU daily can lower the severity of periodontal disease, according to a longitudinal study (Garcia et al., 2011). Bolstering the case for randomized clinical trials to investigate the potential beneficial effect of vitamin D on periodontal disease. In addition to its function in bone and calcium homeostasis, vitamin D acts as an anti-inflammatory agent by inhibiting immune cell cytokine expression and causing monocyte/macrophages to secrete antibiotic-like molecules ( Liu et al., 2006; Cannell et al., 2008a; Cannell et al., 2008b; White, 2008). In truth, vitamin D insufficiency has been related to a higher risk of infectious diseases (Zittermann, 2003). Vitamin D appears to be useful in the treatment of periodontitis, not only because of its direct impact on bone metabolism, but also because it may have antibiotic properties against periodontopathogens and diminish inflammatory mediators involved in tissue destruction (Cochran, 2008).

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