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Evaluation of Hormonal and Immune Changes in Pregnant Woman with Gingivitis

Noor Nemia Hafed, and Jafar Abbas Fadel Al-Maamori

Department of Biology, College of Science, Wasit University, Wasit, Iraq.

Abstract

Pregnancy is accompanied by marked hormonal and immunological changes that may influence oral tissues and increase susceptibility to gingival inflammation. Gingivitis is commonly observed among pregnant women and is often aggravated by these physiological alterations. Therefore, this study evaluated hormonal and immunological changes in pregnant women with gingivitis compared with healthy pregnant and healthy non-pregnant women. The study included three groups, pregnant women with gingivitis, healthy pregnant women, and healthy non-pregnant women. Besides serum levels of reproductive hormones including FSH, LH, estradiol, progesterone, and prolactin, as well as inflammatory cytokines were measured and analyzed using one-way ANOVA. Estradiol, progesterone, and prolactin were significantly higher, whereas FSH and LH were lower in pregnant women. Inflammatory cytokines were also significantly elevated in pregnant women with gingivitis, indicating increased susceptibility to gingival inflammation during pregnancy for maternal and fetal.

Keywords: Estradiol (E2), progesterone (pg/P4), and prolactin.

1. Introduction

Pregnancy represents a unique physiological condition characterized by extensive systemic adaptations that support fetal growth and development while maintaining maternal homeostasis. These adaptations involve coordinated changes in the cardiovascular, endocrine, metabolic, renal, and immune systems, which begin early after conception and progress throughout gestation [1]. Among these changes, hormonal fluctuations play a central role in modulating maternal tissues, including the oral cavity. Gingivitis is considered the most common oral alteration observed during pregnancy. The condition is

primarily associated with variations in estrogen and progesterone levels, which influence oral microbial composition and host immune responsiveness.

During pregnancy, progesterone concentrations may increase up to tenfold, while estrogen levels can rise to thirtyfold compared with non-pregnant states. These hormonal elevations contribute to increased vascular permeability, enhanced gingival crevicular fluid flow, and heightened inflammatory responses within gingival tissues [2].

Fluctuations in estrogen and progesterone during pregnancy result in both reversible and irreversible changes in oral tissues. These changes include dilation and tortuosity of the gingival microvasculature, circulatory stasis, increased vascular permeability, and reduced host immunocompetence. Collectively, these alterations increase the risk of oral infections and inflammatory periodontal conditions during pregnancy [3]. Estrogen has been shown to stimulate gingival fibroblast proliferation, promote connective tissue maturation, and enhance vascular endothelial cell proliferation, thereby intensifying gingival inflammation without a corresponding increase in plaque accumulation [4].

Clinically, gingival changes often become apparent during the second trimester, when the gingiva may appear erythematous, edematous, and prone to bleeding, with symptoms commonly reaching peak severity around the eighth month of gestation [5]. Estrogen and progesterone exert regulatory influences on the hypothalamic pituitary gonadal axis. Elevated estrogen levels during pregnancy can suppress the secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) through negative feedback mechanisms [6].

Following delivery, plasma FSH levels generally return to baseline within approximately two weeks, whereas LH secretion may remain suppressed for longer periods, particularly in lactating women [7]. During pregnancy, levels of FSH and LH are markedly suppressed due to elevated concentrations of estrogen, progesterone, and human chorionic gonadotropin (hCG). This hormonal environment prevents follicular development and ovulation, ensuring maintenance of the pregnancy [8].

Periodontal inflammation during pregnancy is also strongly influenced by immunological mechanisms. Bacterial accumulation within gingival tissues activates the innate immune response, leading to the recruitment of macrophages

and other immune cells. These cells release pro-inflammatory cytokines, including interleukin-8 (IL-8), interleukin-1β (IL-1β), and tumor necrosis factor-alpha (TNF-α), which contribute to tissue inflammation and periodontal destruction [9]. The host immune response in periodontal disease involves a complex cytokine network comprising both pro-inflammatory and anti-inflammatory mediators [10].

IL-8 is produced by a variety of immune and inflammatory cells in response to microbial and inflammatory stimuli and plays a critical role in neutrophil activation and chemotaxis toward sites of inflammation [11]. TNF-α and IL-1β are key mediators in the early stages of inflammation, enhancing the recruitment of monocytes, macrophages, and neutrophils to affected periodontal tissues. Elevated levels of these cytokines are closely associated with increased tissue damage and disease severity in periodontal conditions [12].

2. Methodology

All clinical examinations were carried out under the supervision of a qualified dentist. The study population consisted of women aged from 16 to 40 years who were clinically and laboratory evaluated for periodontal status. Participants were divided into three groups.

The first group included fifty pregnant women diagnosed with gingivitis following clinical periodontal examination. These participants exhibited one or more clinical signs, including gingival redness, swelling, tenderness, bleeding during brushing or flossing, plaque and calculus accumulation, periodontal pocket formation, halitosis, and dental caries. The second group consisted of fifteen healthy pregnant women with clinically healthy gingiva. The third group also included fifteen healthy non-pregnant women who were free from periodontal and systemic diseases and served as controls. Women with systemic diseases that could influence oral health, those receiving medications affecting periodontal condition, individuals who had recently used antibiotics or anti-inflammatory drugs, and obese participants were excluded from the study. All control participants were in good general health and showed no clinical signs of periodontal disease.

2. 1 Blood Samples Collection

Venous blood samples (5 mL) were collected from the antecubital vein of each participant using sterile disposable syringes. Samples were collected in gel tubes, then

centrifuged at 5000 rpm for 10 minutes to separate serum. Obtained serum samples were stored at -20 °C until further biochemical and immunological analyses were performed.

2. 2 Hormonal and Immunological Assays

Serum concentrations of reproductive hormones, including follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), progesterone, and prolactin, were determined for all study participants. In addition, serum levels of inflammatory cytokines, namely interleukin-1β (IL-1β), interleukin-8 (IL-8), and tumor necrosis factor-alpha (TNF-α), were measured using standard immunoassay techniques according to the manufacturers' instructions.

2. 3 Statistical Analysis

Data were collected, summarized, analyzed, and presented using the statistical package for social sciences (SPSS) version 26. The numerical data were presented as (mean ± standard deviation) after performing the Kolmogorov-Smirnov normality test to determine the distribution pattern. A chi-square test as well as a one-way ANOVA test was applied for data, and Duncan's multiple range comparisons (DMRTs) were used to assess differences among groups. Besides, Pearson's correlation was used to evaluate the relationship between two numerical variables. The P-value of < 0.05 was considered statistically significant [13].

3. Results

Biochemical analysis of serum samples revealed marked alterations in reproductive hormone levels among the study groups. Estradiol (E2), progesterone, and prolactin concentrations were significantly higher in both groups of pregnant women, including those with gingivitis and healthy pregnant women, compared with healthy non-pregnant women ($P < 0.001$). No statistically significant differences were observed between pregnant women with gingivitis and healthy pregnant women regarding these hormones.

In contrast, serum levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) were significantly lower in both pregnant groups when compared with healthy non-pregnant women ($P < 0.001$). These findings indicate a pregnancy-related suppression of gonadotropin secretion, irrespective of gingivitis status. The detailed distribution of hormonal parameters among the three study groups are listed in table 1.

Table 1: Levels of hormones E2, progesterone, prolactin, FSH, and LH.

Group	Pregnant with gingivitis		Healthy Pregnant		Healthy non-Pregnant		p-value
Parameters	Mean± SD	Range	Mean ± SD	Range	Mean ± SD	Range	
E2 (pg/mL)	1608.18± 134.2^{A}	420.0-3212.00	1919.13± 156.9^{A}	810.00-3000.00	14.15 ± 1.49^{B}	7.20-20.30	0.001**
Progesterone (ng/mL)	41.25±8.2^{A}	14.46-60.0	41.76 ± 8.6^{A}	23.20-58.00	11.90 ± 3.01^{B}	5.00-23.50	0.001**
Prolactin (ng/mL)	142.3±44.5^{A}	24.90-361.40	123.5 ± 26.7^{A}	36.22-207.40	10.06 ± 2.8^{B}	4.40-18.10	0.001**
FSH (mIU/mL)	1.06 ± 0.12^{A}	0.30-3.10	0.7 ± 0.11^{A}	0.40-2.30	5.48 ± 1.1^{B}	3.10-8.60	0.001**
LH (mIU/mL)	0.39 ± 0.06^{A}	0.30-0.60	0.37 ± 0.05^{A}	0.30-0.50	2.83 ± 0.23^{B}	1.30-4.10	0.001**

SD: standard deviation; †: one way ANOVA; **: significant at $P < 0.05$.

3. 1 Immunological Parameters

Analysis of inflammatory cytokines demonstrated significant variations among the study groups. Serum interleukin-8 (IL-8) levels were significantly elevated in both groups of pregnant women compared with healthy non-pregnant women ($P < 0.001$), reflecting an overall increase in inflammatory activity associated with pregnancy. However, IL-8 levels were higher in pregnant women with gingivitis than in healthy pregnant women.

Serum interleukin-1β (IL-1β) concentrations were significantly higher in pregnant women with gingivitis compared with both healthy pregnant and healthy non-pregnant women ($P < 0.001$). Similarly, tumor necrosis factor-alpha (TNF-α) levels were significantly elevated in pregnant women with gingivitis relative to the other two groups ($P < 0.001$). These results indicate an enhanced inflammatory response associated with periodontal involvement during pregnancy. The detailed cytokine profiles for all study groups are summarized in table 2.

Table 2: Levels of hormones IL-1β, IL-8, and TNF-α.

Group	Pregnant with gingivitis		Healthy Pregnant		Healthy non-Pregnant		p-value
Parameters	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD	Range	
IL-1β(pg/mL)	0.25 ± 0.08^{A}	0.12-0.61	0.18 ± 0.005^{B}	0.18-0.20	0.14 ± 0.012^{B}	0.12-0.16	0.001**
IL-8(pg/mL)	0.33 ± 0.07^{A}	0.21-0.65	0.26 ± 0.01^{B}	0.23-0.27	0.20 ± 0.03^{C}	0.15-0.32	0.001**
TNF-α (pg/mL)	0.34 ± 0.06^{A}	0.21-0.55	0.28 ± 0.09^{B}	0.24-0.65	0.24 ± 0.03^{B}	0.18-0.32	0.001**

SD: standard deviation; †: one way ANOVA; **: significant at $P < 0.05$.

4. Discussion

During pregnancy, hormonal fluctuations and the placenta's production of elevated estrogen levels lead to increased vascular permeability and blood flow in gingival tissues, accompanied by altered immunological responses. These changes play a vital role in regulating the physiological and hormonal adaptations that prepare the mother's body to support the growing fetus [14]. Estradiol modulates the immune system by inhibiting specific immune cell functions and altering the synthesis of inflammatory cytokines. This modulation can exacerbate gingival inflammation by reducing the body's ability to combat the microorganisms responsible for gingivitis [15].

Consequently, estradiol contributes to the redness and swelling of gingiva, which are hallmark features of gestational gingivitis [16]. Progesterone naturally rises during pregnancy due to its production by the corpus luteum and the placenta. Therefore, progesterone levels are expected to be higher in pregnant women compared to non-pregnant women [17]. Progesterone plays an important role in increasing blood flow to the gums and vascular permeability, making gingival tissue more sensitive and susceptible to inflammation and bleeding [18]. These hormonal changes, combined with oral hygiene practices, can enhance the inflammatory response to normal oral bacteria, increasing the likelihood of pregnancy gingivitis even in cases where bacterial levels are like non-pregnant women [19]. Prolactin concentrations were significantly elevated in pregnant women, reflecting increased pituitary activity during pregnancy.

This hormone plays a fundamental role in mammary gland development and lactation and has also been reported to exert immunomodulatory effects that may influence inflammatory processes during pregnancy [20]. The suppression of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) observed in pregnant women is consistent with the physiological inhibition of the hypothalamic pituitary gonadal axis during pregnancy. Elevated estrogen, progesterone, and human chorionic gonadotropin levels exert negative feedback on gonadotropin secretion, preventing follicular maturation and ovulation and maintaining pregnancy stability [21, 22].

The absence of significant differences in FSH and LH levels between pregnant women with and without periodontal disease indicates that these changes are pregnancy-related rather than periodontal-dependent.

The immunological findings of this study demonstrated significantly elevated levels of IL-1β, IL-8, and TNF-α in pregnant women with gingivitis. IL-1β is a key pro-inflammatory cytokine that initiates inflammatory cascades in periodontal tissues and contributes to connective tissue breakdown and bone resorption [23, 24]. Pregnancy-related hormonal modulation may further amplify host reactivity to periodontal pathogens, resulting in increased IL-1β expression [25].

IL-8 plays a central role in neutrophil recruitment and activation at sites of inflammation. Elevated IL-8 levels observed in pregnant women, particularly those with periodontal disease, reflect an enhanced chemotactic response that contributes to gingival tissue inflammation and damage [26], [27]. Findings support the hypothesis that pregnancy amplifies inflammatory responses associated with gingivitis. Tumor necrosis factor-alpha (TNF-α) is a major mediator of inflammation and tissue destruction in gingivitis. Increased TNF-α levels observed in pregnant women with gingivitis indicate a heightened inflammatory burden and may have systemic implications.

Elevated TNF-α has been associated with adverse pregnancy outcomes, including preterm birth, emphasizing the importance of gingivitis diagnosis and management during pregnancy [28].

5. Conclusion

Pregnancy is associated with significant hormonal and immunological changes that influence gingivitis. Elevated levels of estradiol, progesterone, and prolactin, along with reduced follicle-stimulating hormone and luteinizing hormone, reflect normal pregnancy-related adaptations. Pregnant women with gingivitis exhibited increased levels of pro-inflammatory cytokines, indicating an enhanced inflammatory response. The interaction between pregnancy-related hormonal changes and periodontal inflammation may increase gingival tissue susceptibility, highlighting the importance of periodontal care during pregnancy.

6. References

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