

The Influence of Depression on Gingival Health and C-Reactive Protein Among Female Students in Iraq: A Cross-Sectional Study

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Background: Gingival health is considered an important concern in dentistry and can affect people, especially females. Depression plays a crucial role in the gingival state.

Aim of the Study: This study aimed to test the consequences of a depressive state on gingival health status in women in association with C-reactive protein in saliva.

Materials and Methods: A cross-sectional study was conducted using a sample of 500 randomly selected women. All chosen females in the sample suffered from depression, but in different grades, and this was achieved using Beck's Depression Inventory II questionnaire. Plaque and gingival indices were used to assess the oral health. Salivary flow rate and C-reactive protein levels were examined in the high- and low-depression subsamples.

Results: Participants were divided into three grades based on the depression scale (mild, moderate, and severe). The severe depression grades had higher plaque and gingival indices, and the mean C-reactive protein concentration was higher in the severe depression grade, with a highly significant difference ($P=0.000$).

Conclusion: Depression has an actual biological relationship with the health of the oral cavity; it increases gingival inflammatory illnesses and similarly disturbs typical salivary constituents. Increased C-reactive protein levels correlate with psychosomatic depressive illnesses.

Keywords: C-reactive protein, plaque, depression, female, gingivitis, saliva

Introduction

Depression is a common psychiatric illness that leads to persistent feelings of despondency and loss of pleasure during most or all usual activities. This negatively affects emotions and thinking.¹ Depression can have hereditary and environmental causes in addition to environmental factors such as anxiety, traumatic occasions, child abuse concerns, toxic drugs, and different pollutants.²

The Diagnostic and Statistical Manual of Anxiety (DSM-IV) assesses the duration, severity, and progression of sickness. Even so, identifying the illness using these three elements merely offers a slight distinction about an individual who has a probationary experience of depression. Furthermore, depressed individuals may abstain from psychiatric comorbidity-indicative characteristics, such as fear, shock, and different character behavior disturbances. It also obscures diagnosis and management. Nevertheless, the identification of a depressive condition may not directly suggest a distinct type of treatment; therefore, the diagnosis may not indicate any exact management or type of treatment.³

The Beck Depression Inventory (BDI) is one of the most well-known self-reported depressive signs and symptoms scales. Construct validity was verified successfully by matching scores with other measures for depression.⁴ It is a decent

tool that enables the assessment of the severity of depression. This denotes that the persons register their replies to the scale test sheet questionnaire without giving spoken responses, and then the inspector analyzes the data.^{4,5}

Oral cavity diseases, such as periodontal disease, are associated with emotional disorders and can directly disturb a limited area of the body built by humans. However, these disease effects disturb the entire body and may have opposing consequences on physical and psychological well-being.⁶ Diseases of periodontal tissues comprise a huge diversity of devastating inflammatory conditions that distress structures that support the teeth, “gingiva, bone, and periodontal ligaments,” which can result in tooth loss. Globally, they are the most common illnesses, with two main diseases, “gingivitis and periodontitis,” according to the 2017 classification of periodontal and peri-implant diseases and conditions that specify periodontal disease.⁷

During late adolescence, depression, poor oral hygiene, and hormonal changes may interact to influence oral health outcomes. Depression has been associated with behavioral changes such as reduced motivation for self-care, irregular eating habits, and increased inflammatory responses. Poor oral hygiene, in turn, can exacerbate local inflammation and bacterial accumulation, further contributing to periodontal problems. Additionally, hormonal fluctuations can increase gingival sensitivity and elevate inflammatory biomarkers, such as C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF- α), potentially intensifying the inflammatory response to plaque accumulation. CRP, which is considered an essential inflammatory biomarker, an acute-phase protein formed by the liver, and is extensively used as an inflammatory marker. Increased protein levels have also been associated with depression. Psychological depression may lead to inflammation by activating the hypothalamic-pituitary-adrenocortical axis and sympathetic nervous system, which release several hormones. These hormones and proinflammatory cytokines released by psychological depression stimulate protein production, including CRP, triggering inflammation.⁸ Since there has been no previous investigation in Iraq regarding depression grade in gingival diseases and CRP among females aged 16–18, the current study was conducted.

Materials and Methods

Study Design

The study design was cross-sectional and was conducted in Baghdad City in Iraq, with a sample comprising 500 arbitrarily chosen females aged 16–18 from secondary high schools, where the study was conducted. The sample was collected between September 1, 2022, and May 5, 2023, when the patient’s consent was obtained from their parents.

Ethics

The research procedures were conducted in accordance with the principles outlined in the Declaration of Helsinki for human studies. Ethical approval was obtained from the ethical research committee of the Al-Rafidain University College/ Dentistry Department, with Ref. Number 16122 on August 20, 2022. This study followed the STROBE checklist for cross-sectional studies.

Inclusion and Exclusion Criteria

The study’s female participants were cooperative, systemically healthy, and free of recent antibiotic, anti-inflammatory drug, or birth control pill use for at least three months. The study eliminated any females who were pregnant or menstruated, had a history of chronic systemic disorders known to be associated with periodontal disease (such as diabetes mellitus, obesity, and smoking), or had a retentive factor for plaque (such as an orthodontic device that affected the poor oral health status because these confounding factors can affect the oral health status, specifically the periodontal health status (plaque index)).^{9–13}

Study Sample Population and Distribution

The sample comprising 500 arbitrarily chosen females aged 16–18 from secondary high schools in Baghdad City in Iraq, they were selected using a simple random sampling technique to ensure representativeness, then the sample was divided using Beck’s Depression Inventory (BDI2)⁴ into 3 groups depending on the degree of depression severity (mild,

moderate, and severe). It comprises 21 items reflecting the specific cognitive, affective, and physical symptoms of depression. Each item included four statements that varied in their description of symptom severity. Each question has four scores (0,1,2,3), with a score of “3” indicating severe symptoms and a “0” indicating an absence of the condition; so, the total score is the sum of all responses, where the maximum score that may be achieved for the entire test is sixty-three and score of 0 would be the lowest possible result.

In this study, all the included female were invited to complete the questionnaire on their own. The total scores for depression were considered normal if the scores were 1–10, 11–20 were considered mild, 21–30 was considered moderate, 30–40 was considered severe, and extreme if > 40 . After completing a questionnaire with 500 females, 227 females had mild depression, 163 females had moderate depression, and 110 females had severe depression. Subsequently, only 90 females were arbitrarily selected from mild and severe depression grades (45 females for each) to compare particular oral and salivary investigations using an enzyme-linked immunosorbent assay (ELISA) kit containing 96 samples. This number was determined based on considerations related to cost, resource availability, and laboratory capacity. Furthermore, this sample size was considered sufficient to provide adequate statistical power for detecting differences in CRP levels among the depression severity groups, while ensuring the feasibility of sample collection and processing.

The randomization of the chosen 90 females was performed by the lottery using the lottery method. All 227 mild females were assigned numbers from 1 to 227, written on paper, and placed in their first black bag. All 110 severe females were given numbers from 228 to 337, written on paper, and placed in the second black bag, and 45 numbers were randomly chosen from both bags, where saliva was taken from those females only in this study.

To evaluate oral health, the basic procedures of the 1997 World Health Organization Survey were carried out.¹⁴

Collection of Saliva

Unstimulated saliva was collected in the morning (9–12 AM) to assess baseline salivary composition by comfortably seating each participant with eyes open, head tilted slightly forward for five minutes by the passive drooling method, and asking the subject to (let the saliva drop) into sterilized screw-capped tubes.¹⁵ After collection, the salivary flow rate was expressed in milliliters per 5 min,¹⁶ and the sample was then chilled in a tiny box. The sample was aspirated into a polycarbonate centrifuge test tube and spun at 3000 rpm for 10 min to remove cellular debris from salivary supernatants. Salivary fluid samples were centrifuged, removed from cellular debris, and then frozen at -20°C for enzyme-linked immunosorbent assay (ELISA) analysis within 4 h of collection.

The ELISA machine was a standard ELISA reader device (Human, Germany), using an ELISA Kit (Shanghai Yehua Biological Technology, China) to estimate the CRP concentration (mg/dl). The standard method and technique for preparing the reagent and calculating the results were performed according to the manufacturer’s instructions.

Clinical Examination

In the area adjacent to the margin of the gingiva, dental plaque was assessed using the plaque index of Loe, and inspected and verified gingiva inflammation.¹⁷ All four surfaces of each tooth were scrutinized using a periodontal probe (Hu-Friedy, UK) except 3rd molar and scored (0,1,2,3) for plaque index (score 0: no plaque, score 1: a film of plaque may be recognized only by running a probe across the tooth surface; score 2: moderate plaque that the naked eye can see, score 3: abundance of plaque) and gingival index (score 0: absence of inflammation, score 1: slight color change without bleeding on probing (BOP), score 2: moderate redness, edema, with BOP; score 3: marked redness and ulceration, the tendency to spontaneous bleeding).

The targeted level for the gingival and plaque index was a kappa coefficient value $\geq 75\%$ in five patients to test the reliability measurement of inter- or intra-examiner data between visits.

Statistics

For data analysis, SPSS version 21, SPSS “Statistical Package for Social Sciences” (IBM, USA), was used to estimate the mean and standard error. ANOVA, “One Way Analysis Of Variance” was used with Games-Howell as a post-hoc test to detect differences. Pearson’s correlation coefficient was used to determine the correlation between quantitative

variables. The significance level was nonsignificant (NS) at $P \geq 0.05$, significant (*) at $P < 0.05$, and significant (**) at $P \leq 0.001$.

Results

The sample in the research involved females who are 16–18 years old, selected randomly from schools in Baghdad, CityIraq. Subsamples of 90 females were also chosen randomly from the severe and mild depression grades (45 for mild and 45 for severe depression grades) to create comparisons concerning the analysis of particular oral and salivary variables. For the entire sample, the mild depression grade was higher than the moderate grade and the severity of depression was the lowest (Table 1).

In this study, the P value was statistically significant (NS: Non-significant at $P \geq 0.05$, **: significant at $P \leq 0.001$, *: significance at $P < 0.05$).

Table 1 illustrates the mean values of plaque and gingival indices among females based on severity grades. Analysis of the collected data revealed that the average values of both indices were higher in the severe-grade group. In contrast, the lowest score was among mild depression grades. Statistical differences were significant for both plaque index and gingival health.

Table 2 compares the plaque and gingival indices according to depression grade. There was a significant difference in the comparison of both plaque and the gingival index between mild and severe depression, as well as between moderate and severe depression among females. The other comparisons were not statistically significant.

Table 1 Mean and Standard Error for Gingival and Plaque Indices Among Females According to Depression Grades

Variables	Depression Grades						F	P-value
	Mild (n=227, 45.40%)		Moderate (n=163, 32.60%)		Severe (n=110, 22%)			
	Mean	SE	Mean	SE	Mean	SE		
PLI	1.080	0.029	1.138	0.033	1.295	0.042	9.990	0.000**
GI	0.919	0.027	1.023	0.036	1.152	0.047	9.326	0.000**

Notes: **, significant at $P \leq 0.001$ by one-way ANOVA.

Abbreviations: n, number; SE, standard error; PLI, plaque index; GI, Gingival index; F, F-test.

Table 2 Statistical Differences Amongst Different Depression Grades for Plaque and Gingival Indices Values

Multiple Comparisons				
Games-Howell				
Dependent Variable	Groups		Mean Difference	P-Value
PLI	Mild	Moderate	−0.067	0.258 ^{NS}
		Severe	−0.224	0.000**
	Moderate	Severe	−0.158	0.008**
GI	Mild	Moderate	−0.084	0.128 ^{NS}
		Severe	−0.234	0.000**
	Moderate	Severe	−0.142	0.045*

Notes: NS: Non-significant at $P \geq 0.05$; **, significant at $P \leq 0.001$; *, significant at $P < 0.05$; Games-Howell post-hoc test.

Abbreviations: PLI, plaque index; GI, Gingival index.

Table 3 Mean and Standard Error Values of Salivary C-Reactive Protein to Grades of Depression

Variables	Depression grades				T	df	P-Value
	Mild		Severe				
	Mean	SE	Mean	SE			
CRP	1.398	0.069	2.626	0.143	7.754	88	0.000**

Notes: **, significant at $P \leq 0.001$ by the Paired T-test.

Abbreviations: SE, standard error; T, T-test; df, degrees of freedom; CRP, C-reactive protein.

Table 4 Plaque-Gingival Index Correlation Coefficient with Saliva Flow Rate and C-Reactive Protein Concerning Different Grades of Depression

Depression Grades		SFR		CRP	
		R	P-Value	R	P-Value
Mild	PLI	0.048	0.750	0.159	0.282 ^{NS}
	GI	0.128	0.399	0.179	0.252 ^{NS}
Severe	PLI	0.062	0.688	0.287	0.061 ^{NS}
	GI	0.034	0.830	0.360	0.015*

Notes: NS: Non-significant at $P \geq 0.05$; *, significant at $P < 0.05$ by person correlation coefficient test.

Abbreviations: PLI, plaque index; GI, Gingival index; SFR, Salivary flow rate; CRP, C-reactive protein; R, Correlation coefficient.

Table 3 shows the salivary variables and CRP levels according to different grades. The mean CRP values were greater in the high depression grades, with statistically significant differences.

Plaque and gingival indices correlated with salivary flow rate and CRP levels among females, according to the grades of depression, are shown in Table 4. For salivary flow rate, the correlations were non-significant and positive for both depression grades. Concerning CRP, there were non-significant positive correlations for mild depression grade and non-significant for severe depression grade, and showed no statistical significance, except that the correlation of the gingival index of severe depression grade with CRP was significant.

Discussion

Since “Iraq is the most traumatized country of war ever described” and “a majority of the Iraqis would suffer from severe psychological problems throughout their lives”.¹⁸ Since the country has experienced economic hardship and many conflicts, it is unsurprising that all the observed females show signs of depression. Depression in adolescents is common after they experience social rejection, educational difficulties, or peer pressure.^{18–20}

The plaque and gingival indices increased significantly in patients with severe depression. Regarding the comparison assessment between grades, the differences were highly significant. Numerous studies have been proposed to explain the mechanism by which depression is a systemic inflammatory causative factor in the pathogenesis of periodontal disease, as depression supports the “hypothalamic-pituitary-adrenal (HPA) axis” of chronic dysregulation and additionally defines cortisol and adrenal illnesses, as well as immune dysfunction and excess secretion of proinflammatory cytokines such as IL-6, TNF- α , and CRP. These mediators contribute to a state of systemic inflammation of chronic low-grade, which may exacerbate local inflammatory responses in the periodontium. Through these processes, depression may affect the host response to bacterial plaque accumulation and the subsequent activation of immune responses. When combined with the heightened systemic inflammatory state associated with depression, the synergistic effect may accelerate periodontal

deterioration and progression of periodontal disease in patients, resulting in greater gingival inflammation and tissue breakdown. This might be linked to a worse treatment result owing to a delay in wound healing. Changes in health performance such as oral cleanliness, smoking, and nutrition can also be associated with periodontal disease.^{18,19,21,22} Hyposalivation, gingival tissue circulation, and changes in salivary composition caused by antidepressants can worsen periodontitis.⁸

The gingival score was higher in patients with severe depression. This can be explained by changes in hormones (gonadotrophic hormones), as these hormones modify gingival inflammation in response to plaque biofilms and modify the structure of the sub-gingival microbiome.²³ Other studies have proposed that these hormones may exaggerate inflammation through fluid accumulation caused by changes in the capillary permeability of gingival tissues.²⁴ Furthermore, some conditions may modify gingival inflammation, such as smoking, poor hygiene, and emotional and psychological pressure.^{6,25,26}

Numerous immunity markers, such as acute-phase proteins and CRP, can be identified and measured in the fluids of the oral cavity. Circulating CRP levels in the blood have been used clinically as a general inflammation indicator.²⁷ Several studies have focused on the evaluation of CRP in saliva, and the outcomes increase the possibility of using saliva as a minimally invasive alternative to the use of blood as a sample for observing CRP, and levels in oral fluids are strongly and certainly related to the circulation level.²⁸

In the current study, the theory that elevated “CRP levels are associated with symptoms of psychological depression” was verified. The mean value of CRP was significantly higher in females with severe depression than in those with mild depression. However, the causal mechanisms underlying inflammation and depression are not entirely understood. Systemic inflammatory reactions and psychological influences interact via complicated pathophysiological and behavioral mechanisms. Certain studies specify that proinflammatory cytokines might contribute to depression development by the initiation of the “enzyme indoleamine-2, 3-dioxygenase” that leads to reduced serotonin production and increased kynurenic and quinolinic acids production and thus causes increased secretion of glutamate and so decreased creation of trophic factors, as “brain-derived neurotrophic factor”, a factor associated with depression.²⁹ Second, psychological pressure and stress trigger the “hypothalamic-pituitary-adrenocortical axis and sympathetic nervous system,” which causes the release of stress and depressive hormones that trigger the acute-phase response and activate inflammation.³⁰

In this study, plaque and gingival indices were correlated with CRP levels according to depression grade. It was not significantly positive for a low depression grade, as “periodontal disease is a chronic inflammatory disease”.³¹ However, some reasons for the acute inflammatory phase include participation as CRP. Circulating CRP can enter saliva via the fluid in the gingival sulcus, and a high level of CRP in saliva may reflect an unusually high infiltration from the blood due to tissue inflammation.³²

For severe grade depression, a significant correlation was observed between the gingival index and CRP level. However, this was not significant for plaque, as elevated CRP levels were higher in patients with periodontitis than in gingivitis.³³ In the current study, there was only mild to moderate gingivitis in the entire sample; therefore, the degree of inflammation was not severe. However, it has been assumed that the release of cytokines is a mechanism by which periodontal subgingival infections influence immunological and inflammatory responses both locally and systemically. Disintegration of the periodontium and the beginning of an inflammatory response, marked by the production of CRP, were the outcomes. Therefore, CRP levels in the gingival crevicular fluid or serum can increase owing to the effect of periodontal disease on the systemic response.³⁴ Others believe that CRP is locally produced by endothelial cells. It has also been proposed that genetic susceptibility to inflammation can alter CRP levels as a reaction to periodontal damage or systemic disease; therefore, an explanation of the different correlations of CRP levels established in health and disease groups.^{33,35}

However, a limitation of this study was the lack of a cofounder analysis between CPR values and the plaque/gingival index.

Conclusion

The findings of this study indicate a significant association between depression severity and both oral and systemic salivary inflammatory markers. All the examined female students with severe depressive symptoms exhibited higher plaque and gingival indices, as well as elevated C-reactive protein levels, compared to those with mild or moderate depression, with statistically significant differences ($P = 0.000$). Addressing mental health alongside oral hygiene may therefore be crucial in preventing and managing gingival inflammation.

Acknowledgments

The authors would like to thank Mustansiriyah University (www.uomustansiriyah.edu.iq), Baghdad, Iraq, for their support in this study.

Funding

No external funding was received for this study.

Disclosure

The authors declare no conflicts of interest.

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