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The Association of Periodontitis and different BMI categories with Serum Chemerin Levels -: An Observational Case-Control Study

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Abstract

Background: Chemerin is a adipocytes, epithelial cells, endothelium, fibroblasts, and keratinocytes - derived chemotactic protein. This research was focused on possible connections between glycerin in serum, different body mass indexes (BMI), and appearance of the periodic disease. It is speculated that the findings of our work will help to deepen our comprehension of the interplay of adipokines, obesity, and periodontitis.The purpose of this endeavor is to establish the connections between serum chemerin, the value of BMI, and periodontitis to investigate the association between the indexes associated with the increase in obesity and the onset or aggravation of this disease. **Methods:** A total of 118 individuals volunteered to be a part of this research. serum obtained before the clinical investigations was the serum sample taken. participants were distributed into six groups: First group (C): 30 subjects with a normal BMI (18.5-24.9 kg/m^2) and a healthy periodontium; second group (Ov): 30 subjects with an overweight BMI (25–29.9 kg/m^2) and a healthy periodontium; third group (Ob): 30 subjects with an obesity BMI (≥ 30) and a healthy periodontium; fourth group (P): 30 periodontitis patients with a normal BMI (18.5-24.9 kg/m^2); fifth group (P+Ov): 30 periodontitis patients with an overweight BMI (25–29.9 kg/m^2) and sixth group (P+Ob): 30 periodontitis patients with obesity BMI (≥ 30). Evaluation of probe debut (PPD), clinical attachment loss (CAL), and bleeding upon probing (BOP) were the methods used in the periodontal test. **Results:** The findings of the study point out periodontal patients, and in particular, higher body mass index-filled serum levels of chemerin. Among all the study groups, patients with combined very severe obesity and periodontitis (P+Ob) were found to have the highest chemerin levels in their serum. Chemerin (C) of the control group with a weight within the normal range and a healthy area of periodontium was lower in reach. **Conclusions:** The results suggested that chemerin might be a good indicator biomolecule, which would provide information about the disease progress and deterioration, not only in the cases of overweight subjects but most probably in every person affected. may have a healing effect as its inflammatory effect could be counteracted.

Introduction:

Periodontitis is a chronic disease influenced by various factors, including the devastation of the periodontal tissue driven by the host. Periodontitis is closely linked to dysbiotic plaque biofilms (1). Direct tissue damage results from bacterial products present within the plaque. indirect damage as the bacteria stimulates host inflammatory and immune responses. This dual action contributes to the overall pathology of periodontitis (2). The host response in the context of periodontitis involves intricate interactions among various components, including cells, the extracellular matrix, and circulating cytokines and chemokines (3). The Body Mass Index is commonly employed to categorize individuals as underweight ,normal, overweight or obese (4). Obesity and overweight have become major public health issues worldwide(5). Obesity has been observed to have a detrimental impact on the immune response and susceptibility to infections (6). Obesity and overweight were found to be prevalent in Iraq (7). obese people in Iraq have higher rates of severe periodontitis. Periodontitis and obesity may be related(8), though the precise mechanism underlying this relationship is unknown. Other risk factors that may be involved include smoking and age.(9) It is still unclear how precisely obesity damages periodontal tissue. Obesity alters the host's inflammatory and immunological systems, making them more vulnerable.(10). Silva-Boghossian et al. (2018) propose a correlation between obesity and the composition of subgingival biofilm in individuals, irrespective of their periodontal health status (11). Obesity may influence the microbial environment in the subgingival area; an increased BMI is associated with changes in periodontal pathogens (12) and the inflammatory mediators in both the gingival crevicular fluid (GCF) and of periodontitis individuals and healthy individuals (13). Additionally, it implies that periodontitis has an impact on the circulatory levels of certain mediators derived from adipose tissue (14). Changes in inflammatory mediators in the oral environment (GCF) and systemic circulation (serum) may indicate a complex relationship between body weight, adipose tissue-derived signaling molecules, and the inflammatory processes associated with periodontitis (15). The link between obesity and periodontitis likely doesn't arise from a single influencing factor but rather results from the interplay of various factors, including dietary habits, oral health behavior, water fluoridation, and other considerations (16). Adipokines are released by adipose tissue (17) including chemerin. Chemerin is recognized as a chemotactic protein. The chemotactic function of chemerin is an essential aspect of its role in coordinating immune reactions and facilitating the early stages of the body's defense against various challenges, such as infections or inflammatory processes (18). Chemerin plays crucial roles in immunity, adiposity, and metabolism. Its functions are mediated through its three identified receptors. These receptors are involved in transmitting signals that regulate various physiological processes, including immune responses, adipose tissue functions, and metabolic pathways (19). It has a dual function, acting as both a proinflammatory and anti-inflammatory modulator, The specific condition of the biological system may determine whether chemerin promotes or dampens inflammatory responses. Chemerin appears to enhance the chemotaxis of immature dendritic cells and macrophages. suggests that chemerin may be connecting innate and adaptive immunity, contributing to the start of the immune response. Chemerin might demonstrate an anti-inflammatory action by limiting the accumulation of immune cells and stopping the production of proinflammatory cytokines. In a mouse model with acute lung injury, the administration of chemerin led to a decrease in the accumulation of neutrophils and macrophages at inflammatory sites. Furthermore, there was a reduction in the expression of proinflammatory cytokines (20, 21). Previous studies explain the association of chemerin with periodontitis and diabetes mellitus (22), chemerin with periodontitis

and obesity (23), and chemerin with overweight individual (24). This research seeks to define the relationship among serum chemerin levels in individuals with different body mass categories and periodontally healthy or diseased subjects.

Methods

Study design and patient selection

The design of this study was an observational case-control study. It was undertaken at the Periodontics Department of the Dental Hospital, the Dental College at the University of Baghdad, and the Periodontics Department in the Al-Mamoun specialized dental center. Ethical approval was granted from the University of Baghdad on November 20, 2022. Between December 2022 and May 2023, 180 subjects were recruited to take part in this study, The age ranged between 22 and 65 years in all groups males and females. which consisted of 30 subjects with healthy periodontium-normal weight (C) (BMI 18.5-24.9 kg/m2), 30 subjects with healthy periodontium-overweight (Ov) BMI (25 to 29.9 kg/m2), 30 subjects with healthy periodontium-obese (Ob) (BMI≥30), 30 periodontitis patients with normal weight (P) BMI (18.5-24.9 kg/m2), 30 periodontitis patients with overweight (P+Ov) BMI (25 to 29.9 kg/m2), and 30 periodontitis patients with obesity (P+Ob) BMI (≥30). This formula was used to determine the BMI: Weight (kg) / height (m2) is the BMI (25). Each participant was given informed consent before the study began, providing detailed information about the study's objectives and the sampling process. The inclusion criteria for study enrollment included individuals without systemic diseases, not taking any medication in the last three months, and possessing a minimum of 20 natural teeth. Excluded from the study were individuals who smoked or consumed alcohol, those affected by systemic diseases, and participants who underwent periodontal therapy for the previous three months.

Serum collection and outcome measurements

Every participant had a 3 ml blood sample drawn from the cubital fossa using a 5 ml disposable plastic syringe.The collected bl ood was then placed in gel-separating tubes , centrifuged at 3000 RPM using a Hettich EBA 200 centrifuge, and allowed to stand for 10 to 30 minutes. Separated ,labeled , and kept at 20°C, the resultant serum was (26) . use enzyme-linked immune-sorbent assays (ELISA) to measure serum chemerin in a quantitative manner. CLOUD-CLONE CORP (USA) An ELISA kit (catalog number SEA945Hu 96*2) , intended for precise detection of human chemerin concentrations, was used to quantify the amounts of chemerin in serum. The double-antibody sandwich approach was used with the ELISA kit. An antibody specific to chemerin has already been pre-coated on the micro-plate included in this kit. Next, standards or samples are added with a biotin-conjugated antibody specific to chemerin to the corresponding micro-plate fonts. Subsequently, each micro-plate font is filled with Avidin conjugated to Horseradish Peroxidase (HRP) and incubated. Following the addition of the TMB substrate solution, only the wells containing chemerin, , biotin-conjugated antibody and enzyme-conjugated Avidin will exhibit a change in color. The enzyme-substrate reaction is terminated by the addition of sulphuric acid solution and the color change is measured spectro-photo-metrically at awavelengthof450nm ± 10nm. The concentration of chemerin in the samples is then determined by comparing the optical density (O.D). of the samples to the standard curve. The standard curve of chemerin obtained from this process is shown in figure (1).

Case definition and data collection

Prior to the periodontal examination, using a scale and measuring tape, each participant's height and weight were recorded. The participants' weight was classified into three categories based on their body mass index (BMI): normal (BMI: 18.5-24.9 kg/m2), overweight (BMI: 25-29.9), and obese (BMI: ≥30). Using a unc-15 periodontal probe, a calibrated examiner conducted a thorough evaluation of the periodontal health, assessing bleeding on probing (BOP),

probing pocket depth (PPD), and clinical attachment loss (CAL). Every tooth surface was checked for every parameter. According to Tonetti et al. (2018)(27), subjects were diagnosed with periodontitis if CAL was found at ≥2 non-adjacent teeth or buccal or oral CAL≥3mm with a pocket>3mm at ≥2 teeth. According to Caton et al. (2018) (1) , healthy participants had intact periodontium (no loss of probing attachment) and BOP<10% as well as PPD≤3mm.

Statistical analysis

The Statistics Package for Social Science (SPSS, version 25) was utilized for statistical analysis, which included both descriptive and inferential statistics. The Shapiro-Wilk test was used to evaluate data normality, and it was discovered that all analyzed variables had a normal distribution among groups. We utilized the chi-square test to assess sex distribution statistically because it is considered categorical data. The remaining parameters were determined to be regularly distributed between healthy and diseased individuals, and because this study comprised six groups, a one-way ANOVA test was performed to evaluate them, Tukey Post-hoc test and Dunnett's T3 to identify which group is the significantly different. Pearson's correlation test was used to assess the correlation between chemerin and several clinical periodontal markers. The statistical tests in this study employed a significance level of $p<0.05$ (28).

RESULTS

180 subjects participated and were allocated into a healthy control group (n = 30), an overweight group (n = 30), an obese group (n = 30), a periodontitis group (n = 30), an overweight periodontitis group (n = 30), and an obese periodontitis group (n = 30). The age ranged between 22 and 65 years in all groups. The highest mean age was found in the (P+Ob) group (50.300±6.829) and the youngest in the (C) group (27.700±3.879). Regarding sex distribution, 58.89% of the total participants were females, while males constituted 41.11%. For age ($p =0.051$) and gender ($p =0.053$), no significant difference was found among all six groups. Table 1 results showed that the lowest mean value of percentage of BOP was in the Ov group and increased in the Ob group. The mean values of percentages of BOP in groups with periodontitis (P, P+Ov, and P+Ob) are always increasing, with significant differences in comparison to groups with healthy periodontium (C, Ov, and Ob), respectively. There's also a significant increase in BOP percentage in the (P+Ob) group in comparison to both the (P) group and the (P+Ov) group. Table 2 demonstrates probing pocket depth mean values and clinical attachment level mean values between study groups. Results show that the higher probing pocket depth mean value was found in the (P+Ov) group (4.770±0.463), while it was lower in the (P+O) group (4.620±0.428), and the higher mean value of CAL was found in the (P+Ov) group (3.933±0.809), while it was lower in the (P) group (3.647±0.911), but with no significant difference between them. Table 3 demonstrates an increase in chemerin levels in periodontitis with an increase in BMI. The mean value of the chemerin (C) group was 7.130±2.260 and increased significantly in the (P) group (15.794±2.586). This study also resulted in an increase in the levels of chemerin in the Ov group compared to the C group. Furthermore, the (Ob) group showed an increase in chemerin levels in comparison to both the (C) and (Ov) groups. Table 4 demonstrates the correlation of chemerin with all clinical periodontal parameters. the correlation between chemerin and clinical periodontal parameters, no significant correlation was found in all study groups. ($p =0.053$), no significant difference was found among all six groups.

DISCUSSION

The study discusses the relationship between levels of serum chemerin, periodontal health, and different BMI categories. There is a rise in chemerin levels in the (Ov) group against the (C) group. The (Ob) organization demonstrates a rise in chemerin tiers in opposition to the (C) institution and the

(Ov) organization. The look at's comments affords treasured insights into the relationship between one-of-a-kind Body Mass Index (BMI) categories and serum chemerin degrees. The outcomes suggest a gradient of chemerin elevation that aligns with increasing BMI categories. This observation is consistent with the findings of Matern et al. (29) ; there are no research studies or findings that conflict with that. The study findings also indicated a noteworthy increase in the levels of serum chemerin among patients diagnosed with periodontitis when compared to healthy subjects, regardless of both conditions. This observation is consistent with the results reported in Mahmood and Abdulmajeed's study (30). The improved degrees of chemerin in individuals with periodontitis imply a capacity association between this adipokine and the presence of periodontal disorder. This location contributes to a broader knowledge of the position of chemerin in the context of periodontitis and indicates its ability to be used as a biomarker for assessing periodontal health. But it's really worth noting that the observation performed by Jentsch et al. (2017) did not study any exchange in ranges of chemerin in stimulated complete saliva between periodontal and wholesome agencies (24). Adipokines, a collection of molecules released by means of adipose tissue, embody chemerin, a chemotactic protein that initiates the immune reaction. This protein is concerned with guiding immune cells to sites of inflammation, thereby contributing to the body's initial protection mechanisms in the course of immune responses. Functioning as an adipokine (10). Originally recognized as retinoid acid receptor responder 2 or tazarotene-brought on gene 2 protein (31), adipose tissue and skin release chemerin, which features as an immunomodulating agent. It is broken down by using specific inflammatory proteases and then turns on the G-protein-coupled receptor chemokine-like receptor 1 (CMKLR1), which causes natural killer cells, macrophages, and immature dendritic cells to chemotaxis (32). Using a lipopolysaccharide (LPS)-precipitated animal version of acute lung infection, The studies with the aid of Luangsay et al. Established that chemerin administration accelerated macrophage counts whilst reducing neutrophil activation and recruitment. According to Luangsay et al take a look at , these effects point to chemerin and its receptor, CMKLR1, having more than one roles that indicate both proinflammatory and anti-inflammatory sports (12). As an adipokine, chemerin mediates the chemotaxis of dendritic cells and macrophages, so serving as a mediator among innate and adaptive immunity (33). Many facets of the biology of adipocytes and the inflammatory immune reaction are concerned within the strategies of chemerin in weight problems. Chemerin might be involved in the improvement and operation of adipose tissue. The cells known as adipocytes are in rate of storing fat, and Chemerin's stimulation in their differentiation suggests that these cells play a role within the improvement of adipose tissue. Chemerin might also have an impact on how fat molecules are broken down, which may have an impact on how the body shops for and makes use of fat. Adipose tissue infection is understood to be a result of obesity, and chemerin is known to have the capability to attract immune cells to it. This suggests that the inflammatory immune response connected to weight problems may additionally involve chemerin (34). Chemerin concentrations can also affect the pathophysiology of metabolic syndrome. Chemerin concentrations contribute to the underlying physiological disturbances visible in weight problems and metabolic syndrome. Understanding the position of chemerin may additionally have implications for growing strategies to manipulate or prevent those conditions (35). Previously, institutions had been set up among chemerin and diverse metabolic elements, together with adipogenesis (the formation of fat cells), glucose homeostasis (the renovation of blood sugar ranges), meal consumption, and body weight. These institutions, in addition, highlight the significance of chemerin in metabolic regulation. In the mind, mainly the hypothalamus, chemerin may additionally have a role in regulating

the urge for food and energy homeostasis. The hypothalamus integrates signals from the outer edge, including adipokines like chemerin, to modulate tactics related to food intake and standard strength balance (36). Patients with periodontitis exhibit elevated levels of chemerin in their gingival tissues, (GCF), and plasma. Compared to healthy individuals, those with chronic periodontitis (CP) had higher levels of chemerin and inflammatory cytokines in their serum and GCF, such as interleukin-1β (37), interleukin-6 (38), and tumor necrosis factor-α (39). This positive correlation between chemerin levels and periodontitis inflammation processes suggests a possible link between chemerin and these inflammatory processes. Özcan et al show that chemerin may draw immune cells to the site of inflammation via ChemR23 receptors, thereby aiding in the pathogenesis of periodontitis (40). Chemerin can be a ability remedy target for chronic periodontitis CP due to the fact to its consequences on periodontal ligament stem cells, or PDLSCs. Chemerin is concerned within the acceleration of inflammatory reactions related to periodontal disorder (CP); it also inhibits the osteogenic (bone-forming) differentiation of periodontal ligament stem cells; and because it's far important for retaining tooth guide, abnormalities in its feature can be connected to periodontal disorders. Chemerin has the potential to deal with persistent periodontitis as well. Chemerin focused on might also affect PDLSC osteogenic differentiation and inflammatory responses, which may additionally effect how chronic periodontitis develops (26). Diabetes mellitus was included in the 2018 classification of periodontal disease by the American Academy of Periodontology (AAP) and the European Federation of Periodontology (EFP) as a risk factor contributing to the disease's progression (41). This addition highlights the important influence of diabetes on periodontal health (16). According to Wu et al study , obesity is thought to be a risk factor for the development of type 2 diabetes mellitus (T2DM) (42). This emphasizes the well-established link between inflammation associated with obesity and periodontitis, with inflammatory markers released by adipose tissue—like chemerin—possibly playing a role in the onset or aggravation of the disease. Chemerin controls the degrees of seasoned-inflammatory cytokines such as TNF-α and interleukin-1β (IL-1β). The migration of immature dendritic cells, monocytes, and macrophages to the site of infection through the ChemR23 receptor facilitates chemo-attractant motion of chemerin. It can consequently be determined in inflammatory tissues and fluids (43). Examined the cells known as vascular endothelium. Chemerin has been tested to sell irritation while it activates endothelial nitric oxide synthase (eNOS) at high concentrations. Chemerin may additionally have anti-inflammatory effects at low doses and pro-inflammatory outcomes at high ones (44). Chemerin raises MMP levels, causing pro-inflammatory cytokines and irreversible tissue damage (45). Patients with periodontitis may also have multiplied chemerin tiers, which shows that this marker is extra accurate in figuring out adverse periodontal ailment. Consequently, screening for dangerous periodontal disorder in huge populations may be achieved with chemerin (46)

Study limitation

The study acknowledges limitations, including the use of BMI, which may not accurately reflect visceral fat accumulation, and the case control study design limiting the establishment of causation. And six group study may also have an impact on the outcome. The recommendation for the future is to use waist circumference (WC) as a measure of obesity and conduct the same research methodology with two groups or four considering the age range.

Conclusion

The study found a strong link between greater serum chemerin levels, periodontitis, and a high body mass index. Both periodontitis and BMI cause an increase in the chemerin adipokine concentration. The findings point to a potential link between obesity-related

factors, like a higher BMI, and the development or aggravation of periodontitis. Elevated amounts of chemerin could be a factor in this correlation. Chemerin may be used as a diagnostic biomarker to evaluate periodontal health, particularly in those with higher body mass index. In some groups, elevated chemerin levels may be a sign of a higher risk of the onset or progression of periodontal disease. Furthermore, by understanding how chemerin contributes to periodontal inflammation, novel host-modulation-based therapeutic approaches may be developed.

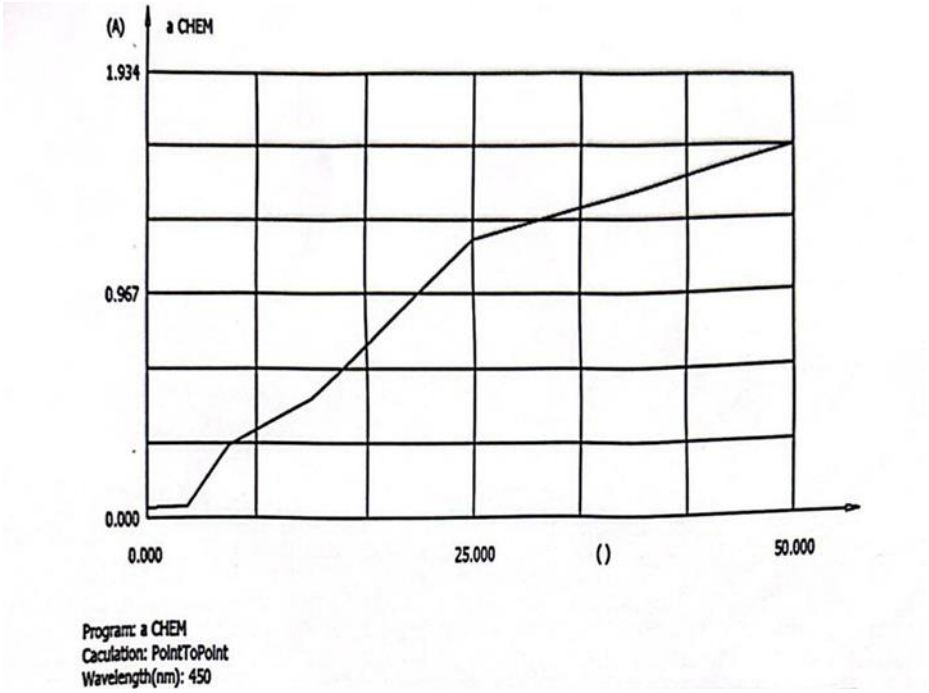

Figure (1) The standard curve of chemerin

Table 1: Descriptive and statistical tests of the mean±SD of BOP among groups using the one-way ANOVA test and independent T test.

Healthy periodontium			Periodontitis			T test	P value
	Mean	**±SD**		**Mean**	**±SD**		
C	4.567	2.096	**P**	60.700	17.552	17.393	**0.000**
Ov	4.433	1.888	**P+Ov**	61.600	12.678	24.428	**0.000**
Ob	5.867	2.345	**P+Ob**	72.500	13.104	27.417	**0.000**
F	4.194			6.062			
P value	**0.018**			**0.003**			

Healthy periodontium normal weight (C), healthy periodontium overweight (Ov), healthy periodontium obese * (Ob),periodontitis normal weight (P), periodontitis overweight (P+Ov), periodontitis obese (P+Ob), healthy periodontium (H), periodontitis (PD).

Table 2: Multiple Comparisons of Mean % of BOP among BMI groups using Tukey HSD

(I) Groups	(J) Groups	Mean Difference (I-J)	P value
C	Ov	0.133	0.968
	Ob	-1.300	0.051
Ov	Ob	-1.433	**0.028**
P	P+Ov	-0.900	0.969
	P+Ob	-11.800	**0.007**
P+Ov	P+Ob	-10.900	**0.013**

*Healthy periodontium normal weight(C) , healthy periodontium overweight (Ov), healthy periodontium obese (Ob), periodontitis normal weight (P), periodontitis overweight (P+Ov), periodontitis obese (P+Ob)**.**

Table 3: Descriptive and statistical tests of PPD and CAL among BMI status using the ANOVA test.

Parameters	P	P+Ov	P+Ob	F	P value
PPD (mm)	4.739±0.479	4.770±0.463	4.620±0.428	0.910	0.410 NS
CAL (mm)	3.647±0.911	3.933±0.809	3.925±0.772	1.146	0.323 NS

Periodontitis normal weight (P), periodontitis overweight (P+Ov), periodontitis obese (P+Ob), probing pocket depth (PPD), * and clinical attachment level (CAL).

Table 4: Descriptive and statistical tests of Chemerin among groups using a one-way ANOVA test and an independent T test.

H			PD			T test	P value
	Mean	**±SD**		**Mean**	**±SD**		
C	7.130	2.260	**P**	15.794	2.586	13.817	**0.000**
Ov	11.287	3.535	**P+Ov**	17.153	3.706	6.273	**0.000**
Ob	13.372	1.706	**P+Ob**	21.196	2.219	15.314	**0.000**
F	44.305			28.041			
P value	**0.000**			**0.000**			

Healthy periodontium normal weight (C), healthy periodontium overweight (Ov), healthy periodontium obese * (Ob),periodontitis normal weight (P), periodontitis overweight (P+Ov), periodontitis obese (P+Ob), healthy periodontium (H), periodontitis (PD).

Table 5: Multiple pairwise comparison of Chemerin with different BMI groups using Dunnett's T3

	(I) Groups	(J) Groups	Mean Difference (I-J)	P value
Dunnett's T3	C	Ov	-4.157	**0.000**
		Ob	-6.242	**0.000**
	Ov	Ob	-2.085	**0.017**
Tukey HSD	P	P+Ov	-1.359	0.172
		P+Ob	-5.402	**0.000**
	P+Ov	P+Ob	-4.044	**0.000**

*Healthy periodontium normal weight(C) , healthy periodontium overweight (Ov), healthy periodontium obese (Ob), periodontitis normal weight (P), periodontitis overweight (P+Ov), periodontitis obese (P+Ob).

Table 6: Correlation of chemerin with BOP, PPD, and CAL in all groups using the Pearson correlation coefficient.

Groups		BOP	PPD	CAL
C	R-value	0.031		
	P value	0.872		
Ov	R-value	-0.158		
	P value	0.404		
Ob	R-value	0.069		
	P value	0.716		
P	R-value	-0.227	0.078	0.176
	P value	0.229	0.716	0.352
P+Ov	R-value	-0.180	0.069	-0.015
	P value	0.341	0.716	0.937
P+Ob	R-value	0.279	0.015	-0.115
	P value	0.136	0.939	0.546

Healthy periodontium normal weight (C), healthy periodontium overweight (Ov), healthy periodontium obese * (Ob),periodontitis normal weight (P), periodontitis overweight (P+Ov), periodontitis obese (P+Ob), healthy periodontium (H), periodontitis (PD).

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