# The relationship between periodontal condition and serum levels of resistin and adiponectin in elderly Japanese

R. Furugen[1], H. Hayashida[1], N. Yamaguchi[2], A. Yoshihara[3], H. Ogawa[3], H. Miyazaki[3], T. Saito[1]

[1]Department of Oral Health, Unit of Social Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

[2]Department of Pediatric Dentistry, Division of Oral Health, Growth and Development, Kyushu University Faculty of Dental Science, Fukuoka, Japan

[3]Division of Preventive Dentistry, Department of Oral Health Science, Graduate School of Medical and Dental Sciences, Niigata University, Niigata, Japan.

Running title: Serum resistin and adiponectin levels in periodontitis

Corresponding author: Toshiyuki Saito, D.D.S., Ph.D.

Department of Oral Health, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki 852-8588, Japan

Phone: 81-95-819-7662

FAX: 81-95-819-7665

E-mail: syto@nagasaki-u.ac.jp

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## Abstract

**Background and Objective:** Diabetes and periodontitis are associated with each other. Adipokines, specifically adiponectin and resistin, are secreted from adipocytes and are thought to cause insulin resistance in rodents. Additionally, adiponectin and resistin may play a role in inflammation and immune responses. The aim of this study was to clarify the relationship between serum levels of adipokines and periodontal conditions in elderly Japanese people with and without periodontitis.

**Material and Methods:** A total of 158 Japanese men and women (76 years old) with or without periodontitis were selected for the study. Serum adiponectin, resistin, interleukin-6 (IL-6) and

tumor necrosis factor-α (TNF-α) concentrations were compared between subjects with and without periodontitis.

**Results:** Serum resistin levels and total leukocyte counts in subjects with periodontitis were higher than in control subjects. No significant differences were observed in adiponectin, IL-6 and TNF-α levels between subjects with and without periodontitis. Logistic regression analysis showed that periodontitis with at least one tooth that displayed a probing pocket depth of ≥6 mm was significantly associated with higher serum resistin levels (odds ratio, 2.0; 95% confidence interval, 1.0-4.0). When excluding periodontitis subjects with ≤10% of bleeding on probing and excluding control subjects with >10% bleeding on probing, differences between groups and odds ratio increased. Serum adiponectin tended to decrease in patients with periodontitis, albeit not significantly.

**Conclusion**: Increased serum resistin levels were significantly associated with periodontal condition, especially when considering bleeding on probing, in elderly Japanese people. There was also a trend, though non-significant, toward decreased levels of adiponectin in subjects with periodontitis.

## Introduction

The local host response to periodontopathogens and their products includes the proliferation and release of macrophages and cytokines. These immune components are thought to play a crucial role in periodontitis. Various cytokines, including interleukin-1β and tumor necrosis factor-α (TNF-α), are determinants of the progression of periodontitis (1). Additionally, increased circulating interleukin-6 (IL-6) levels appear to be correlated with disease severity (2).

Recent evidence indicates that periodontitis may have profound effects on systemic health. Several studies have evaluated the relationship between diabetes, metabolic syndrome and periodontal disease (3-6). Most epidemiological evidence indicates that individuals with diabetes tend to have a more rapid progression of periodontitis than non-diabetics (7).

Adipose tissue produces and releases a variety of inflammatory factors, including adiponectin, resistin, leptin and visfatin, as well as cytokines such as TNF-α, IL-6 and monocyte chemoattractant protein-1. These factors and cytokines influence insulin resistance and are thought to play a role in inflammation and immune responses (8). Resistin received its name

from the original observation that it induced insulin resistance in mice. Additionally, resistin is downregulated in mature murine adipocytes cultured in the presence of insulin-sensitizing drugs, including thiozolidinediones (9). Recent studies in humans suggest that very little resistin is expressed in adipocytes; resistin is largely expressed in monocytes, macrophages (10), and bone marrow (11), which are all linked to immune response (8).

In contrast, adiponectin levels are decreased in individuals with obesity, type2 diabetes and cardiovascular disease (12). In addition, adiponectin influences a wide range of inflammatory pathologies, such as rheumatoid arthritis (13). Furthermore, adiponectin inhibits osteoclast formation stimulated by lipopolysaccharide (LPS) from *Actinobacillus actinomycetemcomitans* (14). Regulation of adiponectin is provided by inflammatory cytokines such as IL-6 (15) and TNF-α (16). Inflammatory endotoxins induce resistin in human macrophages via a cascade involving the secretion of inflammatory cytokines such as IL-6 and TNF-α (17). Although altered adipokine levels have been observed in a variety of systemic inflammatory conditions, only a few studies reported an association between periodontitis and adipokines such as leptin and adiponectin. Leptin levels in gingival crevicular fluid decreased as the periodontal disease progressed (18). Although Iwamoto *et al.* demonstrated that periodontal treatment did not influence circulating adiponectin levels (19), a relationship between periodontal conditions and resistin levels has not been examined. Bleeding frequency, which is a direct indicator of gingival inflammation, is considered to be a strong risk factor for the progression of periodontal disease in elderly people (20). Here we investigated the relationship between periodontal conditions and adiponectin, resistin, IL-6 and TNF-α in a population of elderly people.

## Material and methods

### Subjects

In 1998, total 4542 people who were at 70 years old and resided in Niigata, Japan, were sent a written request to participate in the survey and were informed of the purpose of this survey. After two requests, 81.4% (3695) responded positively to participate in the survey. After considering the availability of resources, 600 subjects were randomly selected. The participants signed informed consent forms that described the protocol and were approved by the Ethics Committee of Niigata University Graduate School of Medical Dental Sciences. The methods

used in this study have been described in detail elsewhere (20, 21). Among a total of 418 subjects who attended the 2004 examination, 158 subjects (80 males and 78 females) who were 76 years old and had at least ten teeth with and without periodontitis were selected.

**Periodontal examination**

The periodontal examination included the assessment of probing depth, attachment level (AL) and bleeding on probing (BOP). Parameters were measured at six sites on every tooth. Four trained dentists used calibrated pressured plastic periodontal probes set to give a probing force of 20 g and measured at 1 mm intervals. All functioning teeth were assessed except those that were partially erupted. A calibration of periodontal examination among all dentists was held; κ (kappa value) ranged from 0.81 to 1.00 for probing depth and from 0.74 to 1.00 for AL.

For the selection of subjects, two criteria for periodontal conditions were defined as follows. Model 1: periodontitis, having at least one tooth with a probing pocket depth ≥6mm; and control, having teeth without a probing pocket depth ≥6mm. Model 2: periodontitis with bleeding, excluding subjects with ≤10% of sites with BOP from periodontitis in model 1; control without bleeding, excluding subjects with >10% BOP from control.

A personal interview was conducted to obtain information regarding smoking habits. Body mass index (BMI) was calculated as an indicator of obesity, and subjects were divided into two groups by BMI: normal BMI (< 25.0) and high BMI (≥ 25). Fasting glucose levels were defined as either normal (< 110 mg/dL) or high (≥ 110 mg/dL).

**Enzyme-linked immunosorbent assay (ELISA)**

Blood samples from the anticubital vein were obtained in the morning for measurement of adiponectin, resistin and other biochemical components. All sera were frozen and stored at -80°C until further measurement. Adiponectin, resistin, TNF-α and IL-6 levels in serum samples were examined using ELISA kits KHP0041, KHP0051, KHC3014 and KHC0064 (Biosource International Inc., CA, USA), respectively, according to the manufacturer's protocol. In addition, each plate was checked before use to ensure that the calibration curve measuring the standard was accurate. All samples were run in duplicate. Absorbance of the substrate color reaction was measured using Microplate manager (Bio-Rad Laboratories, Hercules, CA, USA) at

a primary wavelength of 450 nm.

**Data analysis**

Statistical analyses were conducted using SPSS version 12.0J (SPSS Japan, Tokyo, Japan). Quantitative data are presented as the mean ± SD and the median. Statistical significance was estimated using either a chi-squared test or an independent non-parametric test (Mann-Whitney *U*-test). Correlations were calculated using Spearman's rank correlations. Logistic regression analysis was performed to determine the association between periodontitis and the levels of serum resistin and adiponectin. Odds ratios and 95% confidence intervals (CI) were calculated. Each mean value was used as a cut-off point for high or low levels of serum resistin and adiponectin. Adjusted mean values of serum resistin and adiponectin in the subjects with each periodontal condition were calculated by analyses of covariance (ANCOVA), adjusting for sex, smoking, BMI, and fasting glucose levels.

**Results**

Table 1 outlines characteristics of subjects for each periodontal condition. In model 1, there were significantly higher concentrations of total leukocytes (5.96 ± 1.43 vs. 5.46 ± $1.25\times10^3$/μL; $p = 0.015$) and neutrophils (57.78 ± 8.78 vs. 52.88 ± 9.96%; $p = 0.001$) in subjects with periodontitis compared with control subjects. There was a tendency of increased resistin levels and decreased adiponectin levels in periodontitis; however, this difference was not significant. Median values of TNF-α (0.71 vs. 0.60 pg/mL) and IL-6 (0.37 vs. 0.29 pg/mL) were higher in periodontitis patients than in control subjects, albeit not significantly.

Model 2 showed a similar tendency, with significantly higher concentrations of leukocytes (6.25 ± 1.64 vs. 5.44 ± $1.23\times10^3$ / μL; $p = 0.006$) and neutrophils (59.09 ± 9.30 vs. 53.44 ± 9.97%; $p = 0.004$) in subjects with periodontitis with bleeding than in control subjects without bleeding. Additionally, subjects with periodontitis showed significantly higher concentrations of resistin (6.10 ± 3.54 vs. 4.78 ± 2.95 ng/mL; $p = 0.024$) and higher BMI (not significant).

Furthermore, we conducted simple correlation analyses for all subjects between resistin and adiponectin and mean probing pocket depth, mean AL, percentage of BOP, or leukocyte counts (Fig. 1). While resistin levels did not significantly correlate with mean probing pocket

depth and AL (Fig. 1A, B), they were positively correlated with BOP ($r_s$ = 0.198, $p$ = 0.013; Fig. 1C) and leukocyte counts ($r_s$ = 0.233, $p$ = 0.003; Fig. 1D). Adiponectin levels were negatively correlated with mean AL ($r_s$ = -0.212, $p$ = 0.007; Fig. 1F) and leukocyte counts ($r_s$ = -0.316, $p$ < 0.001; Fig. 1H), but not with mean probing pocket depth ($r_s$ = -0.154, $p$ = 0.053; Fig. 1E) nor percentage of BOP (Fig. 1G). Serum levels of resistin and adiponectin were not significantly correlated with IL-6 and TNF-α (data not shown).

Logistic regression analysis was performed using higher resistin levels (≥ 5.3ng/mL) and lower adiponectin levels (< 11.5ng/mL) as dependent variables. These cut-off points were determined using the mean serum levels of all subjects (Tables 2 and 3). Sex, smoking, BMI and fasting glucose levels were used as independent variables. Periodontitis was significantly associated with higher resistin levels both in model 1 (odds ratio, 2.0; 95%CI, 1.0-4.0) and in model 2 (OR, 2.9; 95%CI, 1.2-6.9; Table 2). A BMI of ≥25 was associated with higher resistin levels only in model 2 (odds ratio, 3.2; 95%CI, 1.1-9.4). Although higher BMI correlated negatively with adiponectin as previously reported ($r_s$=-0.245, $p$=0.002), it was not significantly associated with decreased adiponectin levels in multivariate logistic regression analysis (Table 3).

In an analysis of covariance for the same variables as above, i.e. sex, smoking, BMI, and fasting glucose levels, significantly higher resistin levels were observed in subjects with periodontitis with bleeding than in control subjects without bleeding (6.11 ± 0.47 ng/mL vs. 4.78 ± 0.42 ng/mL; Table4). Adiponectin levels were slightly decreased in periodontitis and periodontitis with bleeding; however, these differences were not significant.

**Discussion**

Since all subjects used in this study were elderly (76 years old), most individuals (86.1%) had at least one probing pocket depth site ≥4mm. In addition, BOP levels (mean, 10.9%; median, 7.0%) appeared to be much lower than in other reports (22). Bleeding on probing is a reliable indicator of activity in periodontal disease (23) and may also indicate the progression of periodontal disease in community-dwelling elderly non-smokers (20). Therefore, lower BOP levels may indicate that many elderly people with deep probing pocket depth and severe AL have a more stable periodontal condition compared with younger adults.

Among other inflammatory markers that are traditionally used as diagnostic measures to assess infection and inflammation, total leukocyte counts were significantly higher in subjects with periodontitis than in control subjects in this study. Moreover, our results revealed associations between resistin, adiponectin and other inflammatory variables such as leukocyte counts and BOP. Specifically, resistin levels were siginificantly correlated with BOP and leukocyte counts, indicating an existing inflammation. Therefore, we introduced BOP to the criteria of periodontitis and control in model 2. In addition, serum resistin levels were weakly correlated with average probing pocket depth, but not average AL. These results suggest that resistin levels may be associated with inflammatory variables rather than periodontal destruction such as indicated by AL. Although adiponectin levels were negatively correlated with mean AL, this result was most probably due to the lower adiponectin levels observed in males who had severe AL. Adiponectin levels were negatively correlated with leukocyte counts (Fig.1A), which indicates that adiponectin is an anti-inflammatory mediator, as previously reported (24).

In contrast to the commonly held belief that serum IL-6 and TNF-α levels are increased in periodontitis, we found no significant relationship between either serum IL-6 or TNF-α levels and the severity of periodontitis. Interleukin-6 and TNF-α locally delivered to the gingival tissues influence the pathogenesis of periodontal disease (1, 2). However, these cytokines may have little influence on circulating levels of themselves in elderly people. Additionally, TNF-α is produced mainly during the early stages of an acute inflammation, and the production of TNF-α may be decreased in elderly people.

We found that resistin levels, but not adiponectin levels, were associated with periodontal condition and other inflammatory variables. In addition, adiponectin levels were significantly higher in women (12.61 ± 4.95 μg/mL) than in men (10.35 ± 6.04 μg/mL, $p$ =0.011), but resistin levels were not (women, 4.96 ± 2.71 ng/mL; men, 5.53 ± 3.41 ng/mL, $p$ = 0.24). Therefore, we analyzed the relationship between serum adiponectin levels and periodontal condition in men and women separately. However, the results of these analyses did not reach statistical significance (data not shown). As in the case of previous study suggesting that adiponectin does not appear to be influenced by periodontal treatment (19), periodontal conditions were not associated with serum adiponectin levels in our study. Adiponectin levels might not be influenced by LPS stimulation in human, which is different from the situation for leptin (25) and resistin (17, 25).

Circulating adiponectin is present in several forms, including low-, middle- and high-molecular weight adiponectin, which may activate different signal transduction pathways and exert distinct effects (26). Some of these specific forms, such as high-molecular weight adiponectin, may be significantly associated with periodontal inflammation. Further studies to examine the effects of high-molecular weight adiponectin are necessary.

Studies have also indicated an abundance of resistin in peripheral blood mononuclear cells and macrophages, suggesting an important role of resistin in the process of inflammation (8, 10). Circulating resistin levels are elevated in patients with rheumatoid arthritis (27), cardiovascular disease (28, 29) and chronic kidney disease (30). In a previous study, increased resistin promoted endothelial cell activation by endothelin-1 release and upregulated chemokines (28), suggesting that increased resistin is related to cardiovascular disease. Increased resistin levels caused by periodontal inflammation may mediate the relationship between periodontitis and cardiovascular disease.

When BOP was introduced as one of the selection criteria of periodontal condition, the association between periodintitis and resistin became stronger. Additionally, serum resistin levels were associated with periodontitis in middle-aged Japanese women in the Hisayama study (unpublished data). It remains unknown whether periodontal inflammation influences circulating resistin levels in humans; however, inflammatory cells such as monocytes and macrophages present in the periodontal tissue appear to be the major source of resistin. Since inflammatory cytokines such as IL-6, TNF-α and interleukin-1β have an effect on the expression of resistin *in vitro* (31), it is possible that periodontal inflammation influences resistin expression. Resistin expression also increases in concert with the maturation of monocytes into macrophages. Resistin may play a significant role in monocyte-macrophage function (10). In our study, adding monocyte as an independent variable in the logistic regression analysis did not affect the result. This result suggests that total monocytes may have a limited impact on resistin levels. However, when total leukocyte counts were added, the odds ratio of periodontitis was reduced (data not shown). Total leukocyte counts, including macrophage, may be a causal intermediate existing between periodontitis and increased levels of resistin. Indeed, total leukocyte counts were significantly correlated both with mean probing pocket depth ($r_s$=0.212, $p$=0.007) and with percentage of BOP ($r_s$=0.205, $p$=0.01). Recent data indicate that stimulation of macrophages *in*

*vitro* with LPS or proinflammatory cytokines leads to a marked increase in resistin production (17). Furthermore, administration of LPS to humans is associated with dramatically increased circulating resistin levels (25). Therefore, it is possibile that LPS from periodontal pathogenic bacteria influences adipose tissues and macrophages through inflammatory cytokines.

In summary, here we report that serum resistin is associated with periodontal condition independent of sex, smoking, fasting glucose and BMI. Additionally, this association becomes stronger when BOP is included in the model. It is not clear how serum resistin is associated with periodontal inflammation. Further studies are required to clarify these mechanisms.

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*Table 1.* Characteristics of subjects with and without periodontitis.

| Model 1[a] | Periodontitis (n=84) | | Control (n=74) | | |
|---|---|---|---|---|---|
| | Mean ± SD | Median | Mean ± SD | Median | $P^b$ |
| Periodontal condition | | | | | |
| Probing pocket depth (mm) | 2.52 ± 0.44 | 2.44 | 1.77 ± 0.21 | 1.76 | <0.001 |
| AL (mm) | 3.45 ± 0.88 | 3.26 | 2.77 ± 0.63 | 2.78 | <0.001 |
| BOP (%) | 15.60 ± 12.65 | 10.97 | 5.58 ± 7.32 | 3.25 | <0.001 |
| Adipokine and cytokine level | | | | | |
| Resistin (ng/mL) | 5.58 ± 3.23 | 4.62 | 4.86 ± 2.90 | 4.01 | 0.131 |
| Adiponectin(μg/mL) | 10.92 ± 4.96 | 10.42 | 12.09 ± 6.27 | 10.66 | 0.199 |
| TNF-α (pg/mL) | 0.82 ± 0.74 | 0.71 | 1.19 ± 2.20 | 0.60 | 0.954 |
| IL-6 (pg/mL) | 0.53 ± 0.61 | 0.37 | 0.86 ± 2.15 | 0.29 | 0.273 |
| Blood components | | | | | |
| Leukocyte counts ($\times10^3/\mu L$) | 5.96 ± 1.43 | 5.70 | 5.46 ± 1.25 | 5.30 | 0.015 |
| Platelet ($\times10^4/\mu L$) | 20.27 ± 4.15 | 19.55 | 20.14 ± 4.78 | 19.35 | 0.686 |
| Monocyte (%) | 6.21 ± 1.99 | 5.80 | 6.25 ± 1.72 | 6.10 | 0.650 |
| Neutrophil (%) | 57.78 ± 8.78 | 57.50 | 52.88 ± 9.96 | 52.10 | 0.001 |
| General condition | | | | | |
| Male (%) | 51.2 | | 50.0 | | 0.882 |
| Smoking (%)[c] | 46.4 | | 43.2 | | 0.690 |
| BMI ($kg/m^2$) | 22.77 ± 2.69 | 22.66 | 22.39 ± 2.56 | 22.20 | 0.384 |
| Fasting glucose (mg/dL) | 122.96 ± 39.73 | 114.0 | 118.37 ± 29.58 | 112.0 | 0.409 |

| Model 2 [a] | Periodontitis with bleeding (n=47) | | Control without bleeding (n=60) | | |
|---|---|---|---|---|---|
| | Mean ± SD | Median | Mean ± SD | Median | $p^b$ |
| Periodontal condition | | | | | |
| Probing pocket depth (mm) | 2.65 ± 0.46 | 2.58 | 1.74 ± 0.20 | 1.75 | <0.001 |
| AL (mm) | 3.64 ± 0.89 | 3.50 | 2.70 ± 0.60 | 2.75 | <0.001 |
| BOP (%) | 23.62 ± 11.50 | 20.83 | 2.88 ± 2.67 | 1.93 | <0.001 |
| Adipokine and cytokine level | | | | | |
| Resistin (ng/mL) | 6.10 ± 3.54 | 5.07 | 4.78 ± 2.95 | 3.94 | 0.024 |
| Adiponectin(μg/mL) | 10.85 ± 5.62 | 9.24 | 11.90 ± 6.55 | 10.66 | 0.283 |
| TNF-α (pg/mL) | 0.86 ± 0.80 | 0.84 | 1.22 ± 2.27 | 0.60 | 0.995 |
| IL-6 (pg/mL) | 0.59 ± 0.66 | 0.45 | 0.94 ± 2.31 | 0.32 | 0.272 |
| Blood components | | | | | |
| Leukocyte counts ($\times10^3/\mu L$) | 6.25 ± 1.64 | 6.10 | 5.44 ± 1.23 | 5.30 | 0.006 |
| Platelet ($\times10^4/\mu L$) | 20.92 ± 4.55 | 20.50 | 20.35 ± 4.91 | 19.45 | 0.444 |
| Monocyte (%) | 6.34 ± 2.36 | 5.80 | 6.29 ± 1.74 | 6.10 | 0.751 |
| Neutrophil (%) | 59.09 ± 9.30 | 57.80 | 53.44 ± 9.97 | 52.35 | 0.004 |
| General condition | | | | | |
| Male (%) | 46.8 | | 51.7 | | 0.622 |
| Smoking (%)[c] | 42.6 | | 43.3 | | 0.936 |
| BMI ($kg/m^2$) | 23.01 ± 2.44 | 22.71 | 22.38 ± 2.46 | 22.20 | 0.145 |
| Fasting glucose (mg/dL) | 123.53 ± 43.00 | 113.0 | 117.23 ± 29.94 | 110.0 | 0.398 |

[a]In model 1, the selection criterion of periodontal condition was only with or without ≥6mm of probing depth, whereas in model 2, 10% of BOP was considered a selection criterion in addition to probing pocket depth.

[b]The *p*-values were calculated by Mann-Whitney *U*-test except for percentages of male and smoking by chi-squared test.

[c] Past or current smoking habit.

*Table 2.* Relationship between periodontal conditions and increased resistin level by logistic regression analysis.

| Model 1 | | | | | |
|---|---|---|---|---|---|
| Independent variables | Resistin <5.3ng/ml | Resistin ≥5.3ng/ml | $p$ [a] | Multivariate odds ratio[b] (95%CI) | $p$ |
| Periodontal condition | | | | | |
| Control | 54 (73.0) | 20 (27.0) | 0.066 | 1 | |
| Periodontitis | 49 (58.3) | 35 (41.7) | | 2.00 (1.20-3.98) | 0.046 |
| Sex | | | | | |
| Male | 50 (62.5) | 30 (37.5) | 0.507 | 1 | |
| Female | 53 (67.9) | 25 (32.1) | | 0.43 (0.15-1.21) | 0.109 |
| BMI | | | | | |
| <25 | 87 (66.4) | 44 (33.6) | 0.510 | 1 | |
| ≥25 | 16 (59.3) | 11 (40.7) | | 1.57 (0.64-3.85) | 0.321 |
| Fasting glucose | | | | | |
| <110mg/dL | 43 (63.2) | 25 (36.8) | 0.736 | 1 | |
| ≥110mg/dL | 60 (66.7) | 55 (34.8) | | 0.77 (0.39-1.55) | 0.466 |
| Smoking habit | | | | | |
| No | 56 (64.4) | 31 (35.6) | 0.867 | 1 | |
| Yes | 47 (66.2) | 24 (33.8) | | 0.51 (0.12-1.42) | 0.196 |
| Model 2 | | | | | |
| Independent variables | Resistin <5.3ng/ml | Resistin ≥5.3ng/ml | $p$ [a] | Multivariate odds ratio[b] (95%CI) | $p$ |
| Periodontal condition | | | | | |
| Control without bleeding | 45 (75.0) | 15 (25.0) | 0.024 | 1 | |
| Periodontitis with bleeding | 25 (53.2) | 22 (46.8) | | 2.90 (1.22-6.94) | 0.016 |
| Sex | | | | | |
| Male | 34 (64.2) | 19 (35.8) | 0.840 | 1 | |
| Female | 36 (66.7) | 18 (33.3) | | 0.35 (0.11-1.18) | 0.091 |
| BMI | | | | | |
| <25 | 60 (69.8) | 26 (30.2) | 0.074 | 1 | |
| ≥25 | 10 (47.6) | 11 (52.4) | | 3.18 (1.08-9.38) | 0.036 |
| Fasting glucose | | | | | |
| <110mg/dL | 30 (61.2) | 19 (38.8) | 0.422 | 1 | |
| ≥110mg/dL | 40 (69.0) | 18 (31.0) | | 0.57 (0.23-1.40) | 0.219 |
| Smoking habit | | | | | |
| No | 38 (62.3) | 23 (37.7) | 0.539 | 1 | |
| Yes | 32 (69.6) | 14 (30.4) | | 0.39 (0.12-1.28) | 0.119 |

[a] chi-square test.

[b] odds rario by logistic regression analysis.

*Table 3.* Relationship between periodontal conditions and decreased adiponectin level by logistic regression analysis.

| Model 1 | | | | | |
|---|---|---|---|---|---|
| Independent variables | Adiponectin ≥11.5ng/ml | Adiponectin <11.5ng/ml | $p$ [a] | Multivariate odds ratio[b] (95%CI) | $p$ |
| Periodontal condition | | | | | |
| Control | 34 (45.9) | 40 (54.1) | 0.336 | 1 | |
| Periodontitis | 32 (38.1) | 52 (61.9) | | 1.38 (0.68-2.80) | 0.374 |
| Sex | | | | | |
| Male | 19 (23.7) | 61 (76.3) | <0.001 | 1 | |
| Female | 47 (60.3) | 31 (39.7) | | 0.21 (0.07-0.61) | 0.004 |
| BMI | | | | | |
| <25 | 57 (43.5) | 74 (56.5) | 0.395 | 1 | |
| ≥25 | 9 (33.3) | 18 (66.7) | | 2.21 (0.83-5.92) | 0.114 |
| Fasting glucose | | | | | |
| <110mg/dL | 39 (57.6) | 29 (42.6) | 0.001 | 1 | |
| ≥110mg/dL | 27 (30.0) | 63 (70.0) | | 2.57 (1.26-5.24) | 0.009 |
| Smoking habit | | | | | |
| No | 48 (55.2) | 39 (44.8) | <0.001 | 1 | |
| Yes | 18 (25.4) | 53 (74.6) | | 1.04 (0.36-3.04) | 0.942 |
| Model 2 | | | | | |
| Independent variables | Adiponectin ≥11.5ng/ml | Adiponectin <11.5ng/ml | $p$ [a] | Multivariate odds ratio[b] (95%CI) | $p$ |
| Periodontal condition | | | | | |
| Control without bleeding | 27 (45.0) | 33 (55.0) | 0.321 | 1 | |
| Periodontitis with bleeding | 16 (34.0) | 31 (66.0) | | 1.62 (0.67-3.92) | 0.290 |
| Sex | | | | | |
| Male | 13 (24.5) | 40 (75.5) | 0.002 | 1 | |
| Female | 30 (55.6) | 24 (44.4) | | 0.25 (0.08-0.83) | 0.023 |
| BMI | | | | | |
| <25 | 37 (43.0) | 49 (57.0) | 0.321 | 1 | |
| ≥25 | 6 (28.6) | 15 (71.4) | | 2.20 (0.69-7.04) | 0.182 |
| Fasting glucose | | | | | |
| <110mg/dL | 28 (57.1) | 21 (42.9) | 0.001 | 1 | |
| ≥110mg/dL | 15 (25.9) | 43 (74.1) | | 3.11 (1.30-7.43) | 0.011 |
| Smoking habit | | | | | |
| No | 31 (50.8) | 30 (49.2) | 0.011 | 1 | |
| Yes | 12 (26.1) | 34 (73.9) | | 1.00 (0.31-3.25) | 0.997 |

[a] chi-square test.

[b] odds ratio by logistic regression analysis.

*Table 4.* Adjusted mean value of serum resistin and adiponectin in the subjects with each periodontal condition.

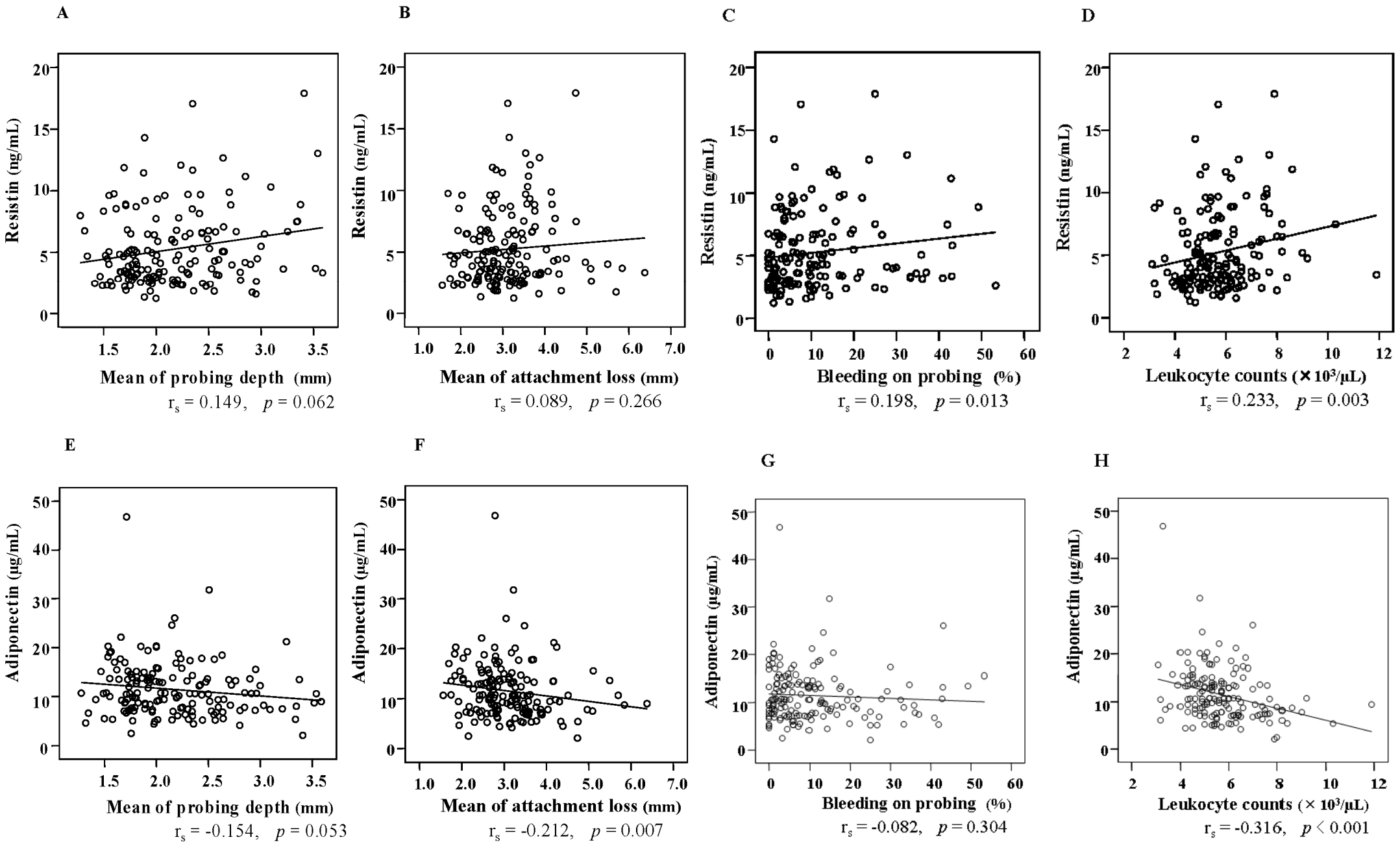
| Periodontal status | n | Resistin | *p* [a] | Adiponectin | *p* [a] |
|---|---|---|---|---|---|
| Model 1 | | | | | |
| Control | 74 | 4.86 ± 0.36[b] | 0.138 | 12.00 ± 0.63 [b] | 0.248 |
| Periodontitis | 84 | 5.59 ± 0.34 | | 11.00 ± 0.59 | |
| Model 2 | | | | | |
| Control without bleeding | 60 | 4.78 ± 0.42 | 0.037 | 11.74 ± 0.76 | 0.551 |
| Periodontitis with bleeding | 47 | 6.11 ± 0.47 | | 11.05 ± 0.86 | |

[a] ANCOVA was performed adjusting for sex, BMI, fasting glucose, and smoking.

[b] mean ± standard error of mean

**Figure legends**

**Fig 1.** Correlations between serum levels of resistin or adiponectin and mean probing depth, mean attachment loss, percentage of bleeding on probing and leukocyte counts. Serum levels of resistin and adiponectin were determined by ELISA. Mean values of probing depth, mean values of attachment loss and percentage of bleeding on probing for each subject were determined by periodontal examination. The figure shows Spearman`s rank correlation analyses between mean probing depth (A), mean attachment loss (**B**), percentage of bleeding on probing (C) and leukocyte counts (D) with serum levels of resistin; also Spearman`s rank correlation analyses between mean probing depth (E), mean attachment loss (F), percentage of bleeding on probing (G) and leukocyte counts (H) with serum levels of adiponectin. $r_s$: Spearman`s rank correlation coefficient


A
Resistin (ng/mL)
Mean of probing depth (mm)
$r_s = 0.149$, $p = 0.062$
B
Resistin (ng/mL)
Mean of attachment loss (mm)
$r_s = 0.089$, $p = 0.266$
C
Resistin (ng/mL)
Bleeding on probing (%)
$r_s = 0.198$, $p = 0.013$
D
Resistin (ng/mL)
Leukocyte counts (×10³/μL)
$r_s = 0.233$, $p = 0.003$
E
Adiponectin (μg/mL)
Mean of probing depth (mm)
$r_s = -0.154$, $p = 0.053$
F
Adiponectin (μg/mL)
Mean of attachment loss (mm)
$r_s = -0.212$, $p = 0.007$
G
Adiponectin (μg/mL)
Bleeding on probing (%)
$r_s = -0.082$, $p = 0.304$
H
Adiponectin (μg/mL)
Leukocyte counts (×10³/μL)
$r_s = -0.316$, $p < 0.001$