

Longitudinal study on the relationship between serum albumin and periodontal disease

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Iwasaki M, Yoshihara A, Hirotsu T, Ogawa H, Hanada N, Miyazaki H. Longitudinal study on the relationship between serum albumin and periodontal disease. J Clin Periodontol 2008; 35: 291–296. doi: 10.1111/j.1600-051X.2008.01215.x.

Abstract

Aim: The purpose of this study was to evaluate the relationship between periodontal disease and the general health status in community-dwelling elderly using the serum albumin concentration as a criterion index of the severity of underlying disease and nutrition.

Material and Methods: Six hundred subjects aged 70 years underwent a baseline examination. Dental examinations were carried out at baseline and once a year for 4 years. Periodontal conditions were estimated for subjects with at least one remaining tooth. Clinical attachment levels at six sites of all teeth present were measured. A change in loss of attachment of 3 mm or greater in 1 year at each site was defined as periodontal disease progression. Data were analysed in subjects for whom data were available for 4 years.

Results: Serum albumin concentration at baseline ranged from 3.4 to 5.0 g/dl with a mean of 4.3 ± 0.2 . When the analysis was stratified by smoking status, we found that serum albumin concentration had a significant effect on periodontal disease progression among non-smokers (standardized regression coefficient = -0.16 ; $p = 0.017$), using multiple regression analysis.

Conclusions: The findings of the present study suggest that serum albumin concentration is a significant risk predictor of periodontal disease progression among elderly non-smokers.

Key words: elderly; longitudinal study; nutrition; periodontal disease; serum albumin

Accepted for publication 17 January 2008

Serum albumin level is a practical marker of the general health status as it demonstrates the severity of an underlying disease and mortality in the elderly (Shibata et al. 1991). Several studies have demonstrated that serum albumin concentrations are associated with general health status among the elderly (Corti et al. 1994, Baumgartner et al.

1996). Moreover, malnutrition may also be monitored by means of serum albumin concentration (Don & Kaysen 2004). Serum albumin is the main protein synthesized by the liver.

Inflammation and malnutrition both reduce albumin concentration by decreasing its rate of synthesis. Chronic diseases are associated with inflammation and the release of inflammatory cytokines such as interleukin-1, interleukin-6, and tumour necrosis factor α , which cause a decrease in serum albumin (Schalk et al. 2004). Albumin concentration is associated with nutrition and inflammation (Kaysen et al. 2002).

On the other hand, periodontitis is defined as an inflammatory condition of the gingival tissues, characterized

by loss of attachment of the periodontal ligament and the bony support of the tooth (Genco et al. 1990). Moreover, periodontitis has been implicated as a risk factor for medical diseases such as cardiovascular diseases and diabetes mellitus (Taylor 2001, D'Aiuto et al. 2004). In periodontal diseases, bacteria trigger inflammatory host responses that cause destruction of the alveolar bone and periodontal connective tissue. The individual characteristics that diminish the efficiency of host response may include medical factors such as malnutrition, which consistently impairs the innate and adaptive defences of the host, including phagocytic function, cell-mediated immunity, complement system, secretory antibody and cytokine

Conflict of interest and source of funding statement

The authors declare that they have no conflict of interests.

This work was supported by a Grant-in-Aid from the Ministry of Health and Welfare of Japan (H10-Iryo-001, H13-Iryo-001 and H16-Iryo-020).

production and function (Enwonwu et al. 2002). According to these studies, malnutrition might intensify the severity of periodontal diseases and lead to their evolution into life-threatening diseases.

Consequently, it is very important to study the association between periodontal disease and serum albumin levels, which reflect the general health status, in the elderly, who may be at a higher risk of developing inflammatory conditions or disorders. However, few studies have demonstrated an important relationship between serum albumin concentration and periodontal diseases; therefore, we adopted the serum albumin concentration as a criterion indicating the general health condition, including nutrition status, and designed this longitudinal study of the relationship between serum albumin and periodontal diseases.

Material and Methods

Subjects

Initially, 4542 (2099 men and 2443 women) Niigata citizens, 70 years old, 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. Considering the availability of resources, examination appointments could be arranged for 600 individuals. The final study sample was randomly recruited from several areas of Niigata in order to have an approximately equal number of men (306) and women (294). All subjects agreed to and signed informed consent forms regarding the protocol, which was reviewed and approved by the Ethics Committee of the Faculty of Dentistry, Niigata University.

None of the subjects was hospitalized or institutionalized. They did not require special care for their daily activities, and had high scores of reliability and validity in a multidimensional 13-item index of competence (TMIG index of competence) (Koyano et al. 1991). The mean score of the TMIG-index subscales of the subjects was 11.9 ± 1.4 . The subjects were recalled and re-examined once a year from 1998 to 2002.

Measurements

Dental examinations were carried out at baseline and once a year for 4 years (1998–2002), that is, five times in 4

years. Periodontal conditions were estimated for subjects with at least one remaining tooth.

Four dentists carried out intra-oral examinations under sufficient illumination using artificial light. The periodontal condition, measured as the clinical attachment level (CAL), was recorded using mouth mirrors and a specially designed pressure-sensitive Vivacare, TPS Probe[®] (Vivacare, Schaan, Liechtenstein). Teeth were probed at six sites per tooth for all teeth present, and measurements were recorded approximately to the nearest whole millimetre.

The examiners were calibrated both before and during the survey using 18 volunteer patients in the University Hospital. As determined by replicate examinations of the attachment level, each percent agreement (± 1 mm) ranged from 70.0% to 100% among four examiners. The κ values ranged from 0.62 to 1.00.

In the longitudinal study, a change in the loss of attachment of 3 mm or greater in 1 year at each site was counted as a periodontal disease event (Brown et al. 1994). Teeth with one disease event were excluded from additional-year assessments. Finally, the numbers of teeth with events over 4 years per person were calculated.

An interview was conducted to obtain information regarding gender and smoking habits. Anthropometric evaluation included measurements of weight and height to calculate body mass index (BMI). In addition, blood pressure levels, biochemical values, such as total protein and calcium, and serum levels of disease markers, such as liver agents (GOT, GPT, and γ -GTP) and immunoglobulin G (IgG), were also evaluated. The serum level of albumin was measured by the bromocresol green albumin (BCG) method.

Statistical analyses

Data were analysed in 304 (164 men, 140 women) subjects examined as dentate in 2002 and in whom the levels of serum albumin were evaluated. Statistical analyses were performed as follows:

Initially, the number of periodontal disease events was considered to be a dependent continuous variable and the unit of analysis was the subject. Gender (male, female), BMI (< 20 , ≥ 20), the highest CAL (< 6 , ≥ 6 mm), number of teeth present (1–9, 10–19, 20–32), blood pressure, serum values of nutritional and

biochemical parameters and serum levels of disease markers were selected as independent variables. Student's *t*-test and analysis of variance (ANOVA) were used to compare the differences. In addition, we defined a serum albumin concentration, ≤ 4.0 g/dl, as low, according to a previous report (Phillips et al. 1989) and compared the number of periodontal disease events between subjects with serum albumin concentrations ≤ 4.0 and > 4.0 g/dl at baseline using Student's *t*-test.

Furthermore, multiple linear regression analysis was used to estimate the effect on periodontal disease events of the serum albumin level while controlling for confounding factors. The number of periodontal disease events was used as a dependent variable, while variables that showed significant relationships with the number of periodontal disease events at $p < 0.05$ in initial analyses were selected as independent variables.

We also compared the number of periodontal disease events between subjects in whom the mean serum albumin concentrations over 4 years were ≤ 4.0 and > 4.0 g/dl. Data were available in 284 (153 men, 131 women) subjects examined as dentate in 2002 and in whom the levels of serum albumin were evaluated.

All analyses were stratified by smoking status to assess effect modification. All calculations and statistical analyses were performed using the STATA[™] software package (Stata Corp. TX, USA).

Results

Overall, 296 subjects dropped out during the study. Among these people, 10 people examined as dentate in 1998 became edentate during this survey. The number of present teeth at baseline was one to three with a mean of 1.5 ± 0.8 . We excluded individuals who dropped out during the study from the statistical analyses. Subjects at 4 years were compared with the same subjects at baseline. Serum albumin concentrations at baseline were 4.3 ± 0.2 g/dl for study subjects and 4.3 ± 0.3 g/dl for the group who dropped out during the study. There was no significant difference between the groups ($p = 0.12$; Student's *t*-test).

The numbers of teeth with a change in the loss of attachment of 3 mm or

Table 1. Relationship between subject characteristics, dental status, blood pressure, serum blood parameters for nutritional and biochemical values, serum disease markers and periodontal disease events

	Non-smokers (N = 165)				Smokers (N = 139)			
	no. of subjects	periodontal disease events*			no. of subjects	periodontal disease events*		
		mean	SD	p-value		mean	SD	p-value
Serum albumin (g/dl)								
>4	145	6.66	4.80	0.0024	119	9.39	5.22	NS†
≤4	20	10.45	7.33		20	10.35	6.30	
Gender								
Male	35	9.03	5.72	0.0155	129	9.74	5.51	NS†
Female	130	6.60	5.07		10	6.90	1.79	
BMI‡								
<20	37	7.27	5.78	NS†	33	10.61	4.92	NS†
≥20	128	7.07	5.17		106	9.20	5.49	
No. of teeth present								
1–9	29	2.62	2.43	<0.0001	16	4.19	2.07	<0.0001
10–19	36	5.75	3.37		44	8.23	3.26	
20–32	100	8.91	5.56		79	11.34	5.86	
Highest CAL§ (mm)								
<6	79	5.57	4.67	0.0003	29	7.17	6.18	0.0074
≥6	86	8.53	5.46		110	10.15	4.99	
High blood pressure								
≤140	115	7.15	4.95	NS†	80	9.76	5.24	NS†
>140	50	7.04	6.05		59	9.22	5.58	
Low blood pressure								
≤90	160	7.11	5.33	NS†	128	9.51	5.38	NS†
>90	5	7.20	4.32		11	9.82	5.56	
GOT								
≤40	162	7.14	5.32	NS†	136	9.59	5.38	NS†
>40	3	6.00	3.61		3	7.00	5.29	
GPT								
≤35	158	7.15	5.33	NS†	133	9.51	5.31	NS†
>35	7	6.29	4.54		6	10.00	7.32	
γ-GTP								
<60	163	7.17	5.30	NS†	127	9.57	5.39	NS†
≥60	2	3.00	1.41		12	9.17	5.39	
IgG (mg/dl)								
<1000	3	12.33	8.08	NS†	9	10.67	4.00	NS†
1000–1900	144	6.94	5.24		121	9.45	5.48	
>1900	18	7.61	5.17		9	9.44	5.46	
Total protein (g/dl)								
<6.5	2	8.00	4.24	NS†	5	8.60	5.18	NS†
≥6.5	163	7.10	5.31		134	9.57	5.40	
Calcium (mEq/l)								
<6.5	55	7.82	5.54	NS†	67	9.63	5.91	NS†
≥6.5	110	6.76	5.16		72	9.44	4.86	

*Number of teeth with periodontal disease progression during 4 years.

†Not significant.

‡Body mass index.

§Clinical attachment level.

greater at each site over 4 years per person were calculated as periodontal disease progression events. The number of events among study subjects was 8.2 ± 5.5 .

We classified participants as smokers or non-smokers based on an interview conducted to obtain information regarding smoking habits. Individuals who reported any smoking history were

considered to be smokers. Among 304 subjects, 139 were considered to be smokers and 165 as non-smokers.

It was found that subjects with 20–32 teeth showed a higher number of periodontal disease events than subjects who had one to nine or 10–19 teeth ($p < 0.0001$). Moreover, subjects who had teeth with CAL ≥ 6 mm showed a high number of periodontal disease

events ($p = 0.0074$). There were no significant differences between gender, BMI, blood pressure, liver agents, IgG, total protein and calcium and periodontal disease events among smokers (Table 1).

On the other hand, it was found that male subjects had a significantly high number of periodontal disease events ($p < 0.0155$). Subjects with 20–32 teeth also showed a higher number of periodontal disease events than subjects who had one to nine or 10–19 teeth ($p < 0.0001$). Moreover, subjects who had teeth with CAL ≥ 6 mm showed a high number of periodontal disease events ($p = 0.0003$). There were no significant differences between BMI, blood pressure, liver agents, IgG, total protein and calcium and periodontal disease events among non-smokers (Table 1).

In addition, subjects with lower serum albumin concentrations (≤ 4.0 g/dl) at baseline had a significantly higher number of periodontal disease events than subjects with higher serum albumin concentrations (> 4.0 g/dl) at baseline (10.5 ± 7.3 versus 6.7 ± 4.8 , respectively; $p = 0.002$, Student's *t*-test) among non-smokers (Table 1 and Fig. 1). Furthermore, subjects with lower mean serum albumin concentrations (≤ 4.0 g/dl) over 4 years had a significantly higher number of periodontal disease events compared with subjects with higher mean serum albumin concentrations during these 4 years (> 4.0 g/dl) (10.4 ± 7.5 versus 6.8 ± 4.8 , respectively; $p = 0.049$, Student's *t*-test) among non-smokers (Fig. 2).

Meanwhile, there was no statistical association between the number of periodontal disease events and serum albumin concentration among smokers (Table 1, Figs 1 and 2).

There was statistically significant interaction between smoking and the numbers of periodontal disease events over 4 years (9.53 ± 5.38 smokers versus 7.12 ± 5.29 non-smokers; $p = 0.0001$, Student's *t*-test). Based on these results, multivariate analyses were stratified by smoking status.

According to the results of the final multiple regression models, serum albumin concentrations at baseline had a significant effect on the number of periodontal disease events (standardized correlation coefficient = -0.16 ; $p = 0.017$), which was independent of other covariates among non-smokers (Table 2).

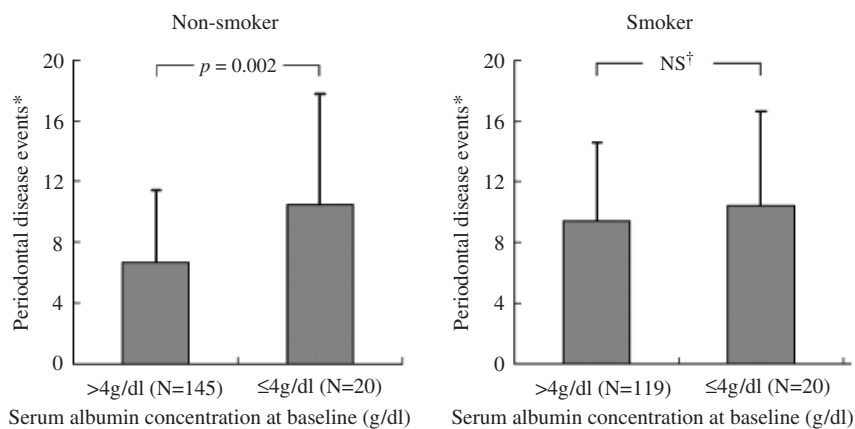


Fig. 1. Relationship between periodontal disease events and serum albumin concentration at baseline, stratified by smoking status. *Number of teeth with periodontal disease progression during 4 years.

†Not significant.

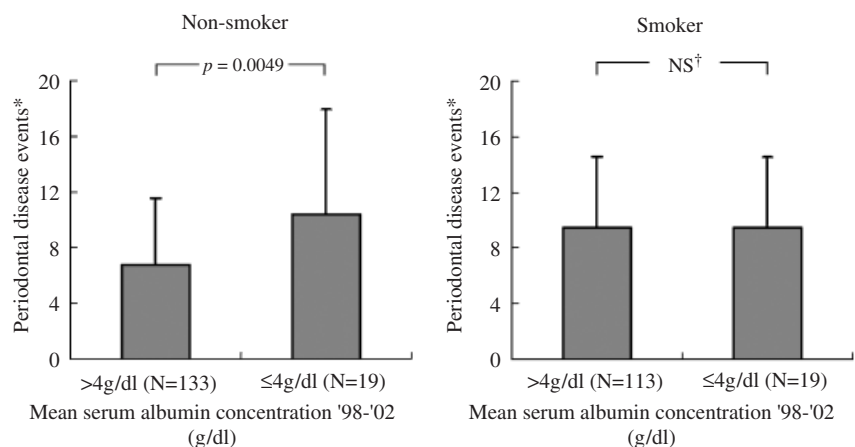


Fig. 2. Relationship between periodontal disease events and the mean serum albumin concentration during 4 years, stratified by smoking status. *Number of teeth with periodontal disease progression during 4 years.

†Not significant.

Discussion

There was no significant difference in serum albumin concentration between subjects who were targeted in this study and those who dropped out; therefore, we thought that subjects in this study were representative of the community.

To our knowledge, this is the first longitudinal study to demonstrate an association between periodontal diseases and serum albumin levels in the elderly. In this longitudinal investigation, a significant association was found between the numbers of periodontal disease events over 4 years and serum albumin levels at baseline in elderly subjects after controlling for confounding factors by multiple linear regression analysis among non-smokers. The standardized regression coefficient of serum

albumin levels at baseline was -0.16 ($p = 0.017$). We observed an inverse independent relationship between the serum albumin concentration and periodontal disease among elderly non-smokers.

Smoking is known to be an effect modifier in periodontal disease (Hyman 2006). In our models, smoking presented as an effect modifier. Therefore, a relationship between serum albumin and periodontal disease might only exist among non-smokers. This suggests that cigarette smoking affects periodontal disease progression considerably. Consequently, there were no significant associations between serum albumin and periodontal disease among smokers. However, we found a significant association between the numbers of

periodontal disease events over 4 years and serum albumin levels among non-smokers.

This relationship might be explained by the possible influence of nutritional aspects (Ogawa et al. 2006). Indeed, several reports have indicated a relationship between the nutritional condition and serum albumin (Magagnotti et al. 2000, Giordano et al. 2001), although some studies have observed an association between nutritional aspects and periodontal disease (Nishida et al. 2000, Amarasena et al. 2005). According to these studies, an unfavourable nutritional status, which indicated lower serum albumin levels, might be responsible for periodontal disease progression.

The serum albumin value might be a good marker for a subject's general health condition. Many conditions, such as malnutrition, inflammatory disorders, liver disease and renal disease, reduce serum albumin levels (Herrmann et al. 1992, Rigaud et al. 2000, Walrand et al. 2000). In these cases, subjects with a low serum albumin concentration are likely to have decreased immunocompetence with an increased risk of infection (Goubran et al. 1996). Measurement of the serum albumin level is a common clinical practice and an important aspect of the general condition of elderly people (Corti et al. 1994).

The relationship between malnutrition and reduced resistance to infection has been suggested by several epidemiologic studies. In malnutrition, most host defence mechanisms are suppressed, especially in reduced cell-mediated immunity. One feasible reason is the reduction in mature fully differentiated T lymphocytes (Nezu & Nakahara 1994). Moreover, malnutrition promotes salivary gland hypofunction, impaired immunity and an early shift in the oral microbial ecology towards a preponderance of anaerobic organisms. Immune suppression impacts negatively on the natural history of inflammatory periodontal diseases (Enwonwu & Sanders 2001). There was a difference between our study and prior studies in the treatment of nutritional status. Unlike our study, prior studies referred to severe malnutrition. This is endemic to our research. Our study subjects might be considered to be biased as they were generally dynamic, independent and non-institutionalized elderly people who volunteered to participate in the survey

Table 2. Multiple linear regression and associated *p*-values

Independent variables	dependent variable Periodontal disease events*					
	coefficient	standard error	<i>p</i> -value	95% CI [†]	standard coefficient [‡]	
Non-smokers						
Serum albumin (g/dl)	-3.54	1.46	0.017	-6.42	-0.65	-0.16
Gender	0.77	0.88	0.385	-0.97	2.50	0.06
No. of teeth present	0.28	0.04	<0.001	0.19	0.36	0.43
Highest CAL [§]	0.60	0.17	0.001	0.26	0.93	0.23
Constant	13.31	6.64	0.047	0.21	26.42	
$R^2 = 0.3005, p < 0.001$						
Smokers						
Serum albumin (g/dl)	-1.08	1.63	0.51	-4.31	2.15	-0.05
Gender	0.91	1.57	0.563	-2.20	4.02	0.04
No. of teeth present	0.34	0.06	<0.001	0.23	0.45	0.47
Highest CAL [§]	0.71	0.19	<0.001	0.34	1.08	0.29
Constant	1.19	7.48	0.874	-13.60	15.98	
$R^2 = 0.2538, p < 0.001$						

*Number of teeth with periodontal disease progression during 4 years.

[†]Confidence interval.

[‡]Standardized coefficients.

[§]Clinical attachment level.

CI, confidence interval.

(Amarasena et al. 2005). It has been observed that such non-institutionalized elderly who are active and independent may be less prone to severe malnutrition than institutionalized elderly who are less active and dependent (Ogawa et al. 2002). Therefore, not severe malnutrition but marginal nutritional deficiencies were most likely to have occurred in our study subjects. Our study suggests that the low serum albumin concentration that indicates depressed general health status, including marginal malnutrition, might be an appropriate marker of periodontal disease progression.

Furthermore, serum albumin can act as an antioxidant in scavenging free radicals (Halliwell & Gutteridge 1990). A low albumin level, therefore, might modulate initial cellular damage and help trigger or enhance the irreversible degenerative processes that are the pathological basis of most inflammatory, ischaemic and proliferative diseases (Corti et al. 1994). Therefore, in terms of the association between serum albumin concentration and periodontal disease, a decreased serum albumin level might directly influence periodontal disease progression.

In this study, serum albumin concentrations ≤ 4.0 g/dl were defined as low, according to Phillips's report (Phillips et al. 1989). In this report, they demonstrated a marked increase in mortality with decreasing serum albumin concentrations that persisted even after adjusting for age, social class, place of

residence, cigarette smoking, serum total cholesterol, serum total calcium and systolic blood pressure. Individuals with < 4.0 g/dl albumin had a crude all-cause mortality rate six times that of men with a serum albumin of 4.8 g/dl or more.

In our study, we selected a 3 mm criterion for an LOA event, according to a previous report (Brown et al. 1994). In this report, they set a change in loss of attachment of 3 mm or more over 18 months as a conservative estimate of actual change taking place.

In conclusion, the findings of the present study suggest that serum albumin concentration is a significant risk predictor of periodontal disease progression among elderly non-smokers. Furthermore, a low serum albumin concentration may impair the periodontal condition.

Acknowledgements

This work was supported by a Grant-in-Aid from the Ministry of Health and Welfare of Japan (H10-Iryo-001, H13-Iryo-001 and H16-Iryo-020).

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Clinical Relevance

Scientific rationale for the study: Investigating the relationship between serum albumin and periodontal disease is important to understand the association between inflammation, nutrition and serum albumin level.

Principal findings: According to the results of multiple regression models, we observed an inverse independent relationship between serum albumin concentration and periodontal disease.

Practical implications: Serum albumin concentration is a significant risk

predictor of periodontal disease progression, especially in the elderly who may be at a higher risk of developing inflammatory conditions or disorders.