

# Association between serum lipid levels and periodontal infection

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## Abstract

**Objective:** The aim of the study was to investigate the association between serum lipids and periodontal infection and the role of serum lipids in the association between body weight and periodontal infection.

**Material and Methods:** The Health 2000 Health Examination Survey, which included 8028 subjects aged 30 or older living in continental Finland. This study was based on a subpopulation of dentate, non-diabetic subjects who had never smoked and were aged under 50 years ( $n = 1297$ ). Periodontal infection was defined as the presence of teeth with deepened periodontal pockets. Serum levels of triglycerides, high-density lipoprotein (HDL)-cholesterol and low-density lipoprotein (LDL)-cholesterol were analysed enzymatically.

**Results:** We found no consistent association between serum lipid levels and periodontal infection among normoweight subjects. There was an association of high serum triglycerides and low HDL with periodontal infection among obese subjects. The association between body mass index and periodontal infection was not essentially affected by serum lipids.

**Conclusion:** In this study population serum lipid levels were not associated with periodontal infection among normoweight subjects. Obese subjects with a high serum triglyceride level and/or a low HDL-cholesterol level could be at higher risk of periodontal infection. Our results suggest that the association between body weight and periodontal infection was mainly mediated through a mechanism other than serum lipids.

Key words: body weight; hyperlipidaemia; periodontal infection

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Hyperlipidaemia is a state of abnormal lipid profile, which is characterized by elevated blood concentrations of triglycerides, elevated levels of total cholesterol and low-density lipoprotein-cholesterol (LDL), and decreased levels of high-density lipoprotein-

cholesterol (HDL). It has been suggested that hyperlipidaemia could be associated with periodontitis, although the role of hyperlipidaemia as a risk factor has not been established (Saito & Shimazaki 2007).

The association between altered lipid profile and periodontitis has been investigated in several studies (Cutler et al. 1999, Lösche et al. 2000, Noack et al. 2000, Katz et al. 2001, 2002, Machado et al. 2005, Moeintaghavi et al. 2005, Vilkuna-Rautiainen et al. 2006, Nibali et al. 2007). The results of these studies, however, are somewhat inconsistent. For example, Katz et al. (2002) reported an association of the scores in the Community Periodontal Index of Treatment Needs (CPITN) with elevated

levels of total cholesterol and LDL-cholesterol and lowered levels of HDL-cholesterol. They found no significant association between triglycerides and CPITN. Lösche et al. (2000), on the other hand, reported significantly higher levels of total cholesterol, LDL-cholesterol and triglycerides in periodontitis subjects as compared with controls, but no difference in HDL-cholesterol levels. Machado et al. (2005) reported no significant differences between the serum lipid levels of periodontitis cases and controls.

Hyperlipidaemia often coexists with obesity (Kopelman 2000) and hyperlipidaemia has been suggested to be one possible mechanism explaining the association between obesity and perio-

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dontitis (Saito & Shimazaki 2007), an association which has been found in several cross-sectional studies in recent years (Saito et al. 2001, Al-Zahrani et al. 2003, Wood et al. 2003, Dalla Vecchia et al. 2005, Genco et al. 2005). This association was also found in this study population (Ylöstalo et al. 2008).

The aim of the present study was, first, to investigate the association between serum levels of triglycerides, HDL-cholesterol and LDL-cholesterol with periodontal infection and, second, to investigate the role of serum lipids as potential mediators in the association between body weight and periodontal infection among an adult population.

## Material and Methods

### Study design

The Health 2000 Health Examination Survey was carried out in 2000 and 2001, conducted by the National Public Health Institute of Finland. The nationally representative survey included 8028 subjects aged 30 or older living in continental Finland. Seventy-nine percent of the sample participated in a health examination and 87% in an interview. Informed consent was obtained from the participants. The study protocol was approved by the ethical committee of Helsinki University Hospital. The data for this survey were collected from clinical oral and health examinations, from laboratory analyses, from self-administered questionnaires and by interviews. Additional information about the Health 2000 Health Examination Survey is available in a published report at <http://www.ktl.fi/terveys2000/julkaisut/baseline.pdf>.

Our study was based on a subpopulation that included dentate, non-diabetic subjects who had never smoked, and who were under 50-years old ( $n = 1297$ ). Diabetic subjects were excluded because of the complex association between diabetes and dyslipidaemia, which may prevent accurate controlling. Diabetes was determined on the basis of information obtained from the health interview and the health examination. Only persons who had not been diagnosed with diabetes by a physician and had no indications of the disease were included into the study population. Basic characteristics of the study population are presented in Table 1.

### Outcome variables

Five calibrated dentists performed clinical oral examinations in a dental chair using a headlamp, mouth mirror and a WHO periodontal probe in line with the WHO instructions. Clinical oral examinations included assessment of the condition of periodontium and teeth.

The primary outcome was existing periodontal infection, defined as the presence of teeth with deepened periodontal pockets. We measured existing periodontal infection with the number of teeth with periodontal pockets of 4 mm or deeper. In addition, we measured periodontal infection also with the number of teeth with periodontal pockets 6 mm deep or deeper. Periodontal pocket depth on probing was measured on four surfaces of each tooth (distobuccal, mid-buccal, mid-oral, mesio-oral), excluding the third molars, and the deepest measurement on each tooth was recorded. The percentual agreement between the examiners and the reference examiner in periodontal pockets was 82% ( $\kappa = 0.32$ ) (Vehkalahti et al. 2004, p. 30).

### Explanatory variables

Serum triglycerides were analysed enzymatically (Olympus System Reagent, Olympus Life Science Research Europa GmbH, Munich, Germany) and HDL-cholesterol and LDL-cholesterol were measured by using direct methods based on immunocomplex separation followed by enzymatic cholesterol determination (Roche Diagnostics, Mannheim, Germany). Triglyceride levels were categorized into quintiles as follows: first quintile,  $<0.80$  mmol/l; second quintile,  $0.80-0.99$  mmol/l; third quintile,  $1.00-1.29$  mmol/l; fourth quintile,  $1.30-1.79$  mmol/l; fifth quintile  $\geq 1.80$  mmol/l. HDL-cholesterol levels were also categorized into quintiles: first quintile,  $<1.09$  mmol/l; second quintile,  $1.09-1.25$  mmol/l; third quintile,  $1.26-1.44$  mmol/l; fourth quintile,  $1.45-1.69$  mmol/l; fifth quintile  $\geq 1.70$  mmol/l. LDL-cholesterol levels were also categorized in the same way: first quintile,  $<2.70$  mmol/l; second quintile,  $2.70-3.16$  mmol/l; third quintile,  $3.17-3.63$  mmol/l; fourth quintile,  $3.64-4.27$  mmol/l; fifth quintile,  $\geq 4.28$  mmol/l.

### Confounding variables

Age was included into the analyses as a continuous variable. Education was categorized into three levels. The lowest cate-

gory included subjects whose education was below high school level and who did not have formal vocational qualifications. The middle category included those who had graduated from high school or vocational school, and the highest category included those with a university degree or who had graduated from polytechnics. Behavioural factors included toothbrushing frequency and dental attendance patterns. Toothbrushing frequency was categorized into three categories as follows: twice a day or more, daily or less frequently. Dental attendance patterns were categorized as follows: those who regularly had dental check-ups *versus* those who used dental services in a symptom-based manner or had never used them.

The presence of dental plaque was measured from three teeth at one surface each as follows: buccal surface from the most posterior tooth on the upper right side, lingual surface from the most posterior tooth on the lower left side and buccal surface from tooth 33. The presence of dental plaque was categorized into three categories (no visible plaque, visible plaque in gingival margins, visible plaque elsewhere) and the highest one was recorded. The use of lipid medication was categorized into three categories (yes/no/missing data). Self-reported frequency of alcohol use was categorized into three categories: none, seldom (once or twice a year to once or twice a month) and often (once a week to 6–7 times a week). We treated alcohol consumption as a continuous variable (estimated amount of alcohol, in grams per week) in the multivariate analysis. The number of teeth (as a continuous variable) was treated as the offset variable in the regression models.

Body weight was assessed by using body mass index (BMI), which is a measure of body weight in relation to height ( $\text{kg/m}^2$ ). Information about weight and height was obtained primarily by means of a clinical examination, but where these data were not recorded in the clinical examination, other sources, such as questionnaires and interviews, were employed. BMI was categorized into quintiles [first quintile,  $<22.4$ ; second quintile,  $22.4-23.9$ ; third quintile,  $23.9-25.8$ ; fourth quintile,  $25.9-28.6$ ; fifth quintile  $>28.6$  (rounded values)].

### Statistical methods

We estimated relative risks and 95% confidence intervals (95% CI) using

the Poisson regression models. The selection of covariates was based on current knowledge of the potential risk factors of periodontal infection. As it is not clear whether BMI should be controlled in the analyses, as lipids may have an effect on periodontium through BMI, we performed a set of multivariate models where BMI was not included as a covariate. In addition, we performed analyses stratified according to BMI.

A stratified two-stage cluster sampling design was used in the survey. Weights were used to correct the effects of non-response. Weighting of sample was based on post-stratification according to gender, age and region. Data analyses were performed using the SUDAAN statistical package to take into account the two-stage cluster sampling design.

## Results

The unadjusted relative risks and their 95% confidence intervals for explanatory variables are presented in Table 2. Unadjusted analysis showed fairly strong exposure-response associations of serum levels of triglycerides, HDL-cholesterol and LDL-cholesterol with the number of teeth with deepened periodontal pockets (4 mm or more). These associations disappeared or at least attenuated markedly after controlling for confounding factors such as gender, age, education, toothbrushing frequency, dental attendance patterns, presence of plaque, lipid medication, alcohol consumption and BMI (Table 3). There was only a slight impact on the estimates when BMI was omitted from the models (Table 3). The unadjusted associations of serum triglyceride and HDL-cholesterol levels with the number of teeth with deep periodontal pockets (6 mm or more) were strong but fairly inconsistent. Also these associations disappeared or attenuated markedly after controlling for confounding factors (Table 3).

The results of the stratified analyses showed no clear association between serum level of triglycerides, HDL-cholesterol or LDL-cholesterol and number of teeth with deepened periodontal pockets among subjects with BMI <25. We noticed elevated estimates with high triglyceride levels and low HDL levels among subjects with BMI 25–<30 and ≥30, but the associations were not consistent (Table 4).

The association of BMI with the number of teeth with deepened periodontal pockets remained consistent,

Table 1. Mean number of teeth with deepened periodontal pockets

	Mean number with standard error (SE)		
	<i>n</i>	teeth with periodontal pockets ≥4 mm	teeth with periodontal pockets ≥6 mm
Total	1297	2.56 (0.16)	0.21 (0.04)
Gender			
Male	509	3.17 (0.24)	0.33 (0.08)
Female	788	2.12 (0.16)	0.12 (0.02)
Age			
30–39 years	679	2.13 (0.16)	0.11 (0.03)
40–49 years	618	3.03 (0.24)	0.32 (0.07)
Education			
Basic	153	3.56 (0.44)	0.54 (0.17)
Intermediate	472	2.74 (0.22)	0.27 (0.07)
Higher	672	2.21 (0.17)	0.09 (0.02)
Toothbrushing frequency			
Twice a day or more often	872	2.40 (0.16)	0.15 (0.03)
Daily	332	2.69 (0.26)	0.31 (0.10)
Less frequently	49	4.91 (0.84)	0.55 (0.23)
Dental attendance pattern			
Regular check-ups	868	2.29 (0.16)	0.11 (0.02)
Irregular	385	3.25 (0.30)	0.42 (0.11)
Presence of plaque			
None	534	1.36 (0.16)	0.06 (0.02)
At gingival margins	645	2.82 (0.18)	0.16 (0.03)
Also elsewhere	115	6.60 (0.74)	1.14 (0.34)
Body mass index (BMI) quintiles			
I (lowest)	259	1.81 (0.19)	0.09 (0.03)
II	259	2.11 (0.26)	0.09 (0.03)
III	260	2.38 (0.24)	0.12 (0.05)
IV	259	2.96 (0.31)	0.27 (0.07)
V (highest)	259	3.50 (0.35)	0.47 (0.14)
Triglyceride quintiles			
I (lowest)	211	2.05 (0.26)	0.13 (0.05)
II	266	2.10 (0.22)	0.19 (0.09)
III	300	2.49 (0.25)	0.17 (0.05)
IV	267	2.71 (0.26)	0.23 (0.06)
V (highest)	249	3.39 (0.36)	0.32 (0.12)
HDL quintiles			
I (lowest)	257	3.40 (0.34)	0.39 (0.14)
II	258	2.57 (0.27)	0.25 (0.07)
III	262	2.52 (0.26)	0.14 (0.05)
IV	258	2.21 (0.25)	0.17 (0.04)
V (highest)	258	2.09 (0.22)	0.09 (0.03)
LDL quintiles			
I (lowest)	256	2.17 (0.24)	0.21 (0.11)
II	261	2.16 (0.24)	0.15 (0.05)
III	257	2.87 (0.30)	0.20 (0.05)
IV	256	2.53 (0.29)	0.22 (0.09)
V (highest)	257	3.10 (0.31)	0.28 (0.08)
Number of teeth			
1–20	54	2.12 (0.48)	0.31 (0.14)
21–25	115	3.03 (0.38)	0.30 (0.09)
More than 25	1128	2.53 (0.17)	0.20 (0.04)
Lipid medication			
No	1174	2.52 (0.18)	0.20 (0.04)
Yes	16	3.18 (0.83)	0.06 (0.06)
Missing data	107	2.88 (0.44)	0.32 (0.20)
Alcohol consumption			
None	111	2.72 (0.51)	0.35 (0.20)
Seldom	654	2.52 (0.20)	0.23 (0.05)
Often	520	2.60 (0.19)	0.16 (0.04)

HDL, high-density lipoprotein; LDL, low-density lipoprotein.

although slightly weakened, after lipids were separately included into the multivariate models (Table 5).

**Discussion**

We found a weak, inconsistent association of serum triglycerides and HDL-cholesterol with the number of teeth with deepened periodontal pockets (4mm or more) in the total study population. However, no consistent associations were observed among normoweight subjects. The association of serum lipids with deep periodontal pockets (6mm or more) showed no consistent association either. Thus, we must point out that our results differ from most previous studies (Cutler et al. 1999, Lösche et al. 2000, Noack et al. 2000, Katz et al. 2001, 2002, Moeintaghavi et al. 2005, Vilkuina-Rautiainen et al. 2006, Nibali et al. 2007), which have mainly shown a fairly strong association between periodontal infection and unfavourable lipid composition.

The discrepancy between the results of this study and the results of the majority of earlier studies deserves attention. We assume that the factors that explain the differences are mainly related to study design, adjustment for confounders and other methodological details. This study is based on a large, representative sample of the general population, unlike most of the above-mentioned studies. Many, but not all, earlier studies were case-control studies, which are subject to various types of bias (Schulz & Grimes 2002). One of them is selection bias, which originates from the lack of comparability between the groups being studied. Selection bias commonly results from procedures used to select subjects and from factors that influence study participation (Rothman & Greenland 1998, p. 119).

We aimed to obtain unconfounded estimates by eliminating the effects of potential confounders, such as smoking, diabetes and age, by restriction. We also adjusted for many confounding factors, such as gender, age, education, toothbrushing frequency, dental attendance pattern, presence of plaque, lipid medication, alcohol consumption and BMI by including them as covariates into multivariate models. All these covariates were associated with the outcome variables, which suggests that they may confound the association

Table 2. Factors related to the number of teeth with periodontal pockets

	n	Teeth with periodontal pockets ≥4 mm		Teeth with periodontal pockets ≥6 mm	
		RR	95% CI	RR	95% CI
Gender	1297				
Male		1.5	1.3–1.7	2.7	1.5–5.1
Female		1.0		1.0	
Age	1297				
30–39 years		1.0		1.0	
40–49 years		1.5	1.3–1.8	3.1	1.6–6.1
Education	1297				
Basic		1.8	1.4–2.4	7.2	3.6–14.3
Intermediate		1.3	1.1–1.5	3.3	1.7–6.2
Higher		1.0		1.0	
Toothbrushing frequency	1253				
Twice a day or more often		1.0		1.0	
Daily		1.1	0.9–1.4	2.0	0.9–4.5
Less frequently		2.1	1.5–2.9	3.8	1.8–7.9
Dental attendance pattern	1253				
Regular check-ups		1.0		1.0	
Irregular		1.4	1.2–1.8	3.7	2.0–6.9
Presence of plaque	1294				
None		1.0		1.0	
At gingival margins		2.1	1.7–2.6	2.7	1.2–6.3
Also elsewhere		4.9	3.7–6.6	19.4	7.8–48.6
Body mass index (BMI) quintiles	1296				
I (lowest)		1.0		1.0	
II		1.2	0.9–1.6	1.0	0.5–2.0
III		1.4	1.1–1.7	1.4	0.5–3.8
IV		1.7	1.3–2.2	3.1	1.4–7.0
V (highest)		2.0	1.6–2.6	5.4	2.4–12.0
Number of teeth	1297				
1–20		1.0		1.0	
21–25		1.4	0.9–2.3	1.0	0.4–2.4
More than 25		1.2	0.8–1.8	0.6	0.3–1.6
Lipid medication	1297				
No		1.0		1.0	
Yes		1.3	0.8–2.2	0.3	0.1–2.0
Missing data		1.1	0.8–1.6	1.6	0.4–5.9
Alcohol consumption	1285				
None		1.1	0.8–1.6	2.3	0.7–8.0
Seldom		1.0	0.8–1.2	1.5	0.8–2.7
Often		1.0		1.0	

Unadjusted relative risks (RR) with 95% confidence intervals (CI).

between serum lipids and periodontal infection. Indeed, these restrictions and adjustments caused a marked attenuation of the unadjusted associations.

One explanation for the association observed in earlier studies, but not in this study, could be inadequate control of confounding factors. It is conceivable that these associations, possibly non-causal in nature, are due to the accumulation of poor health habits, such as unhealthy dietary habits and poor oral habits, for example. This view is supported by the observation that unhealthy dental health habits were associated with high levels of serum total cholesterol and triglycerides and low HDL-cholesterol among a

young adult Finnish population (Ylöstalo et al. 2003).

By restricting the analysis to never smokers, it is possible to eliminate confounding related to the toxic effects of smoking and it also excludes the effects of various behavioural factors related to smoking. The reason for limiting the sample to never smokers is based on the fact that it has been demonstrated that even studies with good adjustment for smoking are biased due to residual confounding related to smoking (Hujoel et al. 2002). By excluding diabetic subjects, the confounding effect of diabetes is removed, which is otherwise difficult to control due to its complex association

Table 3. The relation of serum lipid levels to the number of teeth with periodontal pockets

	Teeth with periodontal pockets $\geq 4$ mm			Teeth with periodontal pockets $\geq 6$ mm	
	unadjusted RR (95% CI)	adjusted* RR (95% CI)	adjusted <sup>†</sup> RR (95% CI)	unadjusted RR (95% CI)	adjusted* RR (95% CI)
	<i>n</i> = 1293	<i>n</i> = 1236	<i>n</i> = 1237	<i>n</i> = 1293	<i>n</i> = 1236
<b>Triglyceride</b>					
(1) Quintile (lowest)	1.0	1.0	1.0	1.0	1.0
(2) Quintile	1.0 (0.8–1.4)	1.0 (0.7–1.2)	1.0 (0.8–1.3)	1.5 (0.5–4.1)	0.8 (0.3–2.0)
(3) Quintile	1.2 (0.9–1.7)	1.1 (0.8–1.4)	1.1 (0.9–1.5)	1.3 (0.6–3.2)	0.6 (0.2–1.6)
(4) Quintile	1.4 (1.0–1.8)	1.0 (0.7–1.3)	1.1 (0.8–1.4)	1.8 (0.7–4.3)	0.5 (0.2–1.6)
(5) Quintile (highest)	1.7 (1.3–2.2)	1.1 (0.6–1.5)	1.2 (0.9–1.6)	2.5 (0.9–6.8)	0.6 (0.2–1.5)
Continuous variable	1.19 (1.09–1.30)	1.06 (0.96–1.17)	1.09 (1.00–1.20)	1.45 (1.05–2.00)	1.24 (0.80–1.93)
	<i>n</i> = 1293	<i>n</i> = 1236	<i>n</i> = 1237	<i>n</i> = 1293	<i>n</i> = 1236
<b>HDL</b>					
(1) Quintile (lowest)	1.6 (1.2–2.1)	1.2 (0.9–1.5)	1.3 (1.0–1.7)	4.3 (1.5–11.8)	1.2 (0.5–2.8)
(2) Quintile	1.2 (0.9–1.6)	1.0 (0.7–1.3)	1.0 (0.8–1.3)	2.7 (1.2–6.5)	0.9 (0.4–2.3)
(3) Quintile	1.2 (1.0–1.6)	1.1 (0.9–1.4)	1.2 (0.9–1.5)	1.5 (0.6–4.2)	0.8 (0.2–2.5)
(4) Quintile	1.1 (0.8–1.4)	1.0 (0.8–1.2)	1.0 (0.8–1.3)	1.8 (0.8–4.1)	1.2 (0.5–2.6)
(5) Quintile (highest)	1.0	1.0	1.0	1.0	1.0
Continuous variable	0.62 (0.47–0.80)	0.84 (0.65–1.09)	0.76 (0.60–0.96)	0.19 (0.05–0.80)	0.58 (0.17–1.94)
	<i>n</i> = 1287	<i>n</i> = 1230	<i>n</i> = 1231	<i>n</i> = 1287	<i>n</i> = 1230
<b>LDL</b>					
(1) Quintile (lowest)	1.0	1.0	1.0	1.0	1.0
(2) Quintile	1.0 (0.8–1.3)	1.0 (0.7–1.3)	1.0 (0.8–1.3)	0.7 (0.2–2.5)	0.7 (0.3–2.0)
(3) Quintile	1.3 (1.0–1.7)	1.1 (0.8–1.4)	1.1 (0.9–1.4)	0.9 (0.3–2.9)	0.6 (0.2–1.5)
(4) Quintile	1.2 (0.9–1.6)	1.0 (0.7–1.3)	1.0 (0.8–1.3)	1.0 (0.3–4.1)	0.6 (0.2–1.7)
(5) Quintile (highest)	1.4 (1.1–1.9)	0.9 (0.7–1.2)	1.0 (0.7–1.3)	1.4 (0.4–4.4)	0.4 (0.1–1.4)
Continuous variable	1.16 (1.06–1.28)	0.99 (0.91–1.08)	1.00 (0.91–1.10)	1.16 (0.69–1.97)	0.77 (0.49–1.20)

Unadjusted and adjusted relative risks (RR) with 95% confidence intervals (CI); HDL, high-density lipoprotein; LDL, low-density lipoprotein.

\*Adjusted for gender, age (continuous variable), education, toothbrushing frequency, dental attendance pattern, presence of plaque, number of teeth (offset variable), lipid medication, alcohol consumption (continuous variable) and body mass index (BMI) (continuous variable).

<sup>†</sup>Adjusted for gender, age (continuous variable), education, toothbrushing frequency, dental attendance pattern, presence of plaque, number of teeth (offset variable), lipid medication and alcohol consumption (continuous variable).

with lipid metabolism. The effect of undiagnosed diabetes is probably small as the exclusion criteria of diabetic subjects in this study were strict – no diagnosed diabetes or any implications of the disease before or during the survey. Lastly, by narrowing the study to subjects aged 30–49, it is possible to partly eliminate age-related confounding that can otherwise be difficult to control.

Another methodological detail that can produce variation in results and possibly explain the differences between the results of this study and previous studies is the difference in how periodontitis is defined. We used a continuous variable to describe periodontal infection whereas Katz et al. (2001, 2002), for example, used CPITN scores and Vilkuna-Rautiainen et al. (2006) serum antibody response against periodontal pathogens for determining periodontitis.

Biological explanations for the association between hyperlipidaemia and periodontal infection have been presented. Noack et al. (2000) assessed

neutrophil respiratory burst by the whole blood chemiluminescence and found significant increases in both chemiluminescence and pocket depth on a group of patients with hyperlipidaemia. They suggested that the association of hyperlipidaemia with periodontitis could be due to the dysfunction of polymorfonuclear leucocytes (PMN-cells).

Obesity has been found to associate with periodontal infection (Saito et al. 2001, Genco et al. 2005), which means that body weight could be a confounding factor in the association between hyperlipidaemia and periodontal infection. Moreover, it is possible that body weight could be a mediating factor through which serum lipids have an effect on periodontium. To study the role of body weight as a mediating factor, we created two sets of models: adjustment including and excluding BMI. In the total study population, further adjustment including BMI attenuated the estimates slightly, which suggests that body weight might be a confounder or that serum lipids may

have a limited effect on periodontium through obesity. If serum lipids did have an effect on periodontium through obesity, adjustment including obesity would not be correct, because controlling for BMI would prevent this mediating mechanism from manifesting itself.

In order to study the role of body weight in this association between serum lipids and periodontal infection more thoroughly, we stratified the data by BMI. In these stratified analyses, we detected no clear association between serum lipid levels and the number of teeth with deepened periodontal pockets (4 mm or more) among subjects with BMI <25. This indicates that the levels of serum triglycerides, HDL-cholesterol and LDL-cholesterol are not associated with periodontal infection among normal-weight subjects. Elevated estimates in the higher categories of BMI (25–<30,  $\geq 30$ ), although the association was not exposure-response dependent, suggests that association between serum lipids and periodontal infection could be modified by body weight. Moreover, the synergistic effect between lipid fractions

Table 4. The relation of serum lipid levels to the number of teeth with deepened periodontal pockets, stratified according to body mass index (BMI)

	Teeth with periodontal pockets $\geq 4$ mm					
	RR	95% CI	RR	95% CI	RR	95% CI
	BMI <25		BMI 25–<30		BMI 30 or more	
	<i>n</i> = 630		<i>n</i> = 431		<i>n</i> = 175	
<b>Triglyceride</b>						
(1) Quintile (lowest)	1.0		1.0		1.0	
(2) Quintile	0.9	0.7–1.3	0.8	0.5–1.3	2.0	0.5–7.1
(3) Quintile	1.1	0.8–1.6	1.0	0.6–1.6	1.5	0.4–5.4
(4) Quintile	0.8	0.6–1.2	1.1	0.6–1.7	1.4	0.4–5.1
(5) Quintile (highest)	0.8	0.5–1.4	1.1	0.7–1.8	1.8	0.5–5.8
Continuous variable	0.92	0.73–1.14	1.10	0.96–1.27	1.05	0.89–1.26
	<i>n</i> = 630		<i>n</i> = 431		<i>n</i> = 175	
<b>HDL</b>						
(1) Quintile (lowest)	1.0	0.6–1.6	1.2	0.8–2.0	2.3	1.1–4.7
(2) Quintile	0.8	0.5–1.4	1.0	0.6–1.6	2.1	1.0–4.7
(3) Quintile	1.0	0.7–1.5	1.2	0.8–1.9	1.8	0.8–3.9
(4) Quintile	1.0	0.8–1.4	1.0	0.6–1.5	1.8	0.7–4.4
(5) Quintile (highest)	1.0		1.0		1.0	
Continuous variable	1.05	0.74–1.49	0.76	0.48–1.21	0.63	0.31–1.29
	<i>n</i> = 629		<i>n</i> = 427		<i>n</i> = 166	
<b>LDL</b>						
(1) Quintile (lowest)	1.0		1.0		1.0	
(2) Quintile	1.0	0.7–1.4	1.2	0.8–1.9	0.4	0.2–0.7
(3) Quintile	1.0	0.7–1.3	1.1	0.7–1.8	0.9	0.5–1.7
(4) Quintile	1.0	0.6–1.5	1.1	0.7–1.7	0.7	0.3–1.4
(5) Quintile (highest)	0.9	0.6–1.5	1.1	0.7–1.6	0.7	0.3–1.4
Continuous variable	1.00	0.87–1.15	1.02	0.89–1.17	0.93	0.79–1.10

Adjusted relative risks (RR) with 95% confidence intervals (CI)\*; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

\*Adjusted for gender, age (continuous variable), education, toothbrushing frequency, dental attendance pattern, presence of plaque, number of teeth (offset variable), lipid medication and alcohol consumption (continuous variable).

and other components of what is known as metabolic syndrome, as suggested earlier by Shimazaki et al. (2007), cannot be ruled out either.

Our research group has previously found an association between body weight and periodontal infection in this study population (Ylöstalo et al. 2008). As obesity and unfavourable lipid composition often coexist, it is possible that the weak association between body weight and periodontal infection could be due to harmful effects of serum lipids. Hence, the second aim of our paper was to study the possible mediating role of serum lipids in the association of obesity and periodontal infection. We detected that the association of BMI with teeth with deepened periodontal pockets did not weaken markedly despite adjusting for serum lipids. This suggests that the effect of body weight on periodontium in this population was mainly mediated through mechanisms other than serum lipids.

#### Strengths and limitations

We used the number of teeth with deepened periodontal pockets as a primary outcome. We used probing depth of 4 mm as a cut-off value, which is often used as a limit for deepened pockets, and we used the number of teeth with probing pocket depth of 6 mm or more as a secondary outcome. The number of teeth with deep pockets (6 mm or more) was low, however, so the risk estimates are subject to large random variation.

The strength of using the number of teeth with deepened periodontal pockets as an outcome variable is that the study focuses not only on the presence but also the extent of the infection of the periodontium at the time of survey. Another advantage in using the number of teeth with deepened periodontal pockets as an outcome variable is that in doing so we were able to avoid problems related to the definition of periodontitis. The use of a continuous

variable reflects the true pattern of periodontal infection better than classifying subjects into two categories based on an arbitrary cut-off point and thus made it possible for us to reduce the effect of misclassification due to measurement error.

One limitation is the cross-sectional nature of the present study. One cannot assess the direction of the relation between assumed cause and effect. Although we detected no clear association between serum lipid levels and periodontal infection, our results do not exclude the possibility that periodontal infection could be associated with the development of hyperlipidaemia. Indeed, it has earlier been suggested that changes in immune cell function caused by periodontitis may cause metabolic dysregulation of lipid metabolism through mechanisms involving pro-inflammatory cytokines (Iacopino & Cutler 2000).

Lastly, our results do not exclude the possibility that different combinations of lipid fractions could have some synergistic effect on periodontium.

#### Conclusions

In this population of non-diabetic subjects aged 30–49, who had never smoked, a weak and inconsistent association of serum levels of triglycerides and HDL-cholesterol, but not LDL-cholesterol, with the number of teeth having pockets greater or equal to 4 mm was found. In the stratified analysis, no clear association was found among normoweight subjects, whereas among obese subjects, a high serum triglyceride level and low HDL-cholesterol were found to be associated with the teeth having deepened periodontal pockets. This suggests that serum triglycerides, HDL-cholesterol or LDL-cholesterol separately are not risk factors for periodontal infection among normoweight subjects, whereas there is a possibility that obese subjects with a high serum triglyceride level and/or low HDL-cholesterol level could run a greater risk of developing periodontal infection.

Our second aim was to examine the mediating role of serum lipids in the association between body weight and periodontal infection. In this case, our results suggest that the effect of body weight on periodontium in this study population was mainly mediated through a mechanism other than serum lipids.

Table 5. The relation of body mass index (BMI) to the number of teeth with periodontal pockets

	Teeth with periodontal pockets $\geq 4$ mm	
	RR	95% CI
	Model 1*	n = 1297
BMI		
(1) Quintile (lowest)	1.0	
(2) Quintile	1.1	0.8–1.5
(3) Quintile	1.1	0.9–1.4
(4) Quintile	1.3	1.0–1.7
(5) Quintile (highest)	1.4	1.1–1.8
Continuous variable	1.03	1.01–1.04
	Model 2†	n = 1236
BMI		
(1) Quintile (lowest)	1.0	
(2) Quintile	1.1	0.8–1.5
(3) Quintile	1.1	0.9–1.4
(4) Quintile	1.3	0.9–1.6
(5) Quintile (highest)	1.3	1.0–1.5
Continuous variable	1.02	1.00–1.04
	Model 3‡	n = 1236
BMI		
(1) Quintile (lowest)	1.0	
(2) Quintile	1.1	0.8–1.4
(3) Quintile	1.1	0.8–1.4
(4) Quintile	1.3	1.0–1.7
(5) Quintile (highest)	1.3	1.0–1.7
Continuous variable	1.02	1.00–1.04
	Model 4§	n = 1230
BMI		
(1) Quintile (lowest)	1.0	
(2) Quintile	1.1	0.9–1.5
(3) Quintile	1.1	0.9–1.4
(4) Quintile	1.3	1.0–1.7
(5) Quintile (highest)	1.4	1.1–1.8
Continuous variable	1.03	1.01–1.04

Adjusted relative risks (RR) with 95% confidence intervals (CI); BMI, body mass index.

\*Adjusted for gender, age (continuous variable), education, toothbrushing frequency, dental attendance pattern, presence of plaque, number of teeth (offset variable), lipid medication and alcohol consumption (continuous variable).

†Adjusted for gender, age (continuous variable), education, toothbrushing frequency, dental attendance pattern, presence of plaque, number of teeth (offset variable), lipid medication, alcohol consumption (continuous variable) and serum triglyceride level (continuous variable).

‡Adjusted for gender, age (continuous variable), education, toothbrushing frequency, dental attendance pattern, presence of plaque, number of teeth (offset variable), lipid medication, alcohol consumption (continuous variable) and serum high-density lipoprotein (HDL)-cholesterol level (continuous variable).

§Adjusted for gender, age (continuous variable), education, toothbrushing frequency, dental attendance pattern, presence of plaque, number of teeth (offset variable), lipid medication, alcohol consumption (continuous variable) and serum low-density lipoprotein (LDL)-cholesterol level (continuous variable).

## References

- Al-Zahrani, M. S., Bissada, N. F. & Borawski, E. A. (2003) Obesity and periodontal disease in young, middle-aged, and older adults. *Journal of Periodontology* **74**, 610–615.
- Cutler, C. W., Shinedling, E. A., Nunn, M., Jotwani, R., Kim, B.-O., Nares, S. & Iacopino, A. M. (1999) Association between periodontitis and hyperlipidemia: cause or effect? *Journal of Periodontology* **70**, 1429–1434.
- Dalla Vecchia, C. F., Susin, C., Rosing, C. K., Oppermann, R. V. & Albandar, J. M. (2005) Overweight and obesity as risk indicators

- for periodontitis in adults. *Journal of Periodontology* **76**, 1721–1728.
- Genco, R. J., Grossi, S. G., Ho, A., Nishimura, F. & Murayama, Y. (2005) A proposed model linking inflammation to obesity, diabetes and periodontal infections. *Journal of Periodontology* **76**, 2075–2084.
- Hujoel, P. P., Drangsholt, M., Spiekerman, C. & DeRouen, T. A. (2002) Periodontitis-systemic disease associations in the presence of smoking – causal or coincidental? *Journal of Periodontology* **73**, 51–60.
- Iacopino, A. M. & Cutler, C. W. (2000) Pathophysiological relationships between

periodontitis and systemic disease: recent concepts involving serum lipids. *Journal of Periodontology* **71**, 1375–1384.

- Katz, J., Chaushu, G. & Sharabi, Y. (2001) On the association between hypercholesterolemia, cardiovascular disease and severe periodontal disease. *Journal of Clinical Periodontology* **28**, 865–868.
- Katz, J., Flugelman, M. Y., Goldberg, A. & Heft, M. (2002) Association between periodontal pockets and elevated cholesterol and low density lipoprotein cholesterol levels. *Journal of Periodontology* **73**, 494–500.
- Kopelman, P. G. (2000) Obesity as a medical problem. *Nature* **404**, 635–643.
- Lösche, W., Karapetow, F., Pohl, A., Pohl, C. & Kocher, T. (2000) Plasma lipid and blood glucose levels in patients with destructive periodontal disease. *Journal of Clinical Periodontology* **27**, 537–541.
- Machado, A. C., Quirino, M. R. & Nascimento, L. F. (2005) Relation between chronic periodontal disease and plasmatic levels of triglycerides, total cholesterol and fractions. *Brazilian Oral Research* **19**, 284–289.
- Moeintaghavi, A., Haerian-Ardakani, A., Talebi-Ardakani, M. & Tabatabaie, I. (2005) Hyperlipidemia in patients with periodontitis. *The Journal of Contemporary Dental Practice* **6**, 78–85.
- Nibali, L., D'Aiuto, F., Griffiths, G., Patel, K., Suvan, J. & Tonetti, M. S. (2007) Severe periodontitis is associated with systemic inflammation and a dysmetabolic status: a case-control-study. *Journal of Clinical Periodontology* **34**, 931–937.
- Noack, B., Jachmann, I., Roscher, S., Sieber, L., Kopprasch, S., Luck, C., Hanefeld, M. & Hoffmann, T. (2000) Metabolic diseases and their possible link to risk indicators of periodontitis. *Journal of Periodontology* **71**, 898–903.
- Rothman, K. J. & Greenland, S. (1998) Precision and validity in epidemiologic studies. In: Rothman, K. J. & Greenland, S. (eds). *Modern Epidemiology*, 2nd edition, pp. 115–134. Philadelphia, PA: Lippincott Williams & Wilkins.
- Saito, T. & Shimazaki, Y. (2007) Metabolic disorders related to obesity and periodontal disease. *Periodontology* **2000** **43**, 254–266.
- Saito, T., Shimazaki, Y., Koga, T., Tsuzuki, M. & Ohshima, A. (2001) Relationship between upper body obesity and periodontitis. *Journal of Dental Research* **80**, 1631–1636.
- Schulz, K. F. & Grimes, D. A. (2002) Case – control studies: research in reverse. *Lancet* **359**, 431–434.
- Shimazaki, Y., Saito, T., Yonemoto, K., Kiyohara, Y., Iida, M. & Yamashita, Y. (2007) Relationship of metabolic syndrome to periodontal disease in Japanese women: the Hisayama study. *Journal of Dental Research* **86**, 271–275.
- Vehkalahti, M., Knuutila, M. & Hausen, H. (2004) Kliinisten mittauksen laadun varmistaminen (Quality assurance of clinical examinations). In: Suominen-Taipale, L., Nordblad, A., Vehkalahti, M. & Aromaa, A.

- (eds). *Suomalaisten aikuisten suunterveys, Terveys 2000 – tutkimus (Oral Health of Finnish Adults, Health 2000 Health Examination Survey)*, pp. 24–32. Helsinki: Publications of the National Public Health Institute.
- Vilkuna-Rautiainen, T., Pussinen, P. J., Roivainen, M., Petäys, T., Jousilahti, P., Hovi, T., Vartiainen, E. & Asikainen, S. (2006) Serum antibody response to periodontal pathogens and herpes simplex virus in relation to classic risk factors of cardiovascular disease. *International Journal of Epidemiology* **35**, 1486–1494.
- Wood, N., Johnson, R. B. & Streckfus, C. F. (2003) Comparison of body composition and periodontal disease using nutritional assessment techniques: Third National Health and Nutrition Examination Survey (NHANES III). *Journal of Clinical Periodontology* **30**, 321–327.
- Ylöstalo, P., Suominen-Taipale, L., Reunanen, A. & Knuutila, M. (2008) Association between body weight and periodontal infection. *Journal of Clinical Periodontology* **35**, 297–304.
- Ylöstalo, P. V., Ek, E., Laitinen, J. & Knuutila, M. L. (2003) Optimism and life satisfaction as determinants for dental and general health behavior – oral health habits linked to cardiovascular risk factors. *Journal of Dental Research* **82**, 194–199.

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### Clinical Relevance

*Scientific rationale for the study:* Serum lipids have been suggested to be associated with periodontal infection. To date, results from earlier epidemiological studies have been inconsistent. Serum lipids have also been suggested to be one possible mediating factor explaining

the association between body weight and periodontal infection.

*Principal findings:* We found no consistent association between serum lipid levels and the number of teeth with deepened periodontal pockets among normoweight subjects in this study population. Nor were serum lipids an essential mediating factor

in the association between body weight and periodontal infection.

*Practical implications:* Special attention should be paid to the way confounding factors are handled when investigating the association of periodontitis with other diseases.