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ORIGINAL RESEARCH

Association Between Number of Missing Teeth and Hyperlipidemia: The TCLSIH Cohort Study

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Background: To explore the association between the number of missing teeth and the prevalence of hyperlipidemia in a Chinese adult population.

Methods: 13,932 adults were investigated in the TCLSIH cohort study. The number of missing teeth was determined at baseline through a self-reported questionnaire, and then classified into three categories: 0, 1–2, and ≥3. We defined hyperlipidemia as total cholesterol (TC) ≥ 5.17 mmol/L or triglycerides (TG) ≥ 1.7 mmol/L or low-density lipoprotein (LDL) cholesterol ≥ 3.37 mmol/L or a self-report of physician-diagnosed hyperlipidemia during follow-up visits. Cox proportional-hazards regression models were employed to assess the relationship between the number of missing teeth and incident hyperlipidemia.

Results: A total of 6756 first-incident cases of hyperlipidemia occurred during 42,048 person-years of follow-up (median follow-up, 4.2 years). After adjusted confounders, multivariable HRs and 95% CI for incident of hyperlipidemia across the categories of missing teeth were as follows: in male participants, 1.00 (reference), 1.10 (0.98, 1.22), and 1.03 (0.91, 1.16) (P for trend = 0.30); in female participants, 1.00 (reference), 1.09 (0.99, 1.19), and 1.18 (1.04, 1.33) (P for trend < 0.01).

Conclusion: The number of missing teeth is associated with an increased risk of hyperlipidemia in female participants but not in male participants. Systemic chronic inflammation may potentially mediate this association.

Keywords: tooth loss, dyslipidemia, epidemiological studies, population health, inflammation

Introduction

Hyperlipidemia, characterized by an imbalance in cholesterol levels, is strongly linked to the development of stroke, myocardial infarction, and other cardiovascular diseases.[1–3] It plays a significant role in the pathogenesis of cardiovascular diseases (CVD), contributing to increased morbidity and mortality rates.[4] Meanwhile, it has a high global prevalence and imposes great challenges on public health and healthcare systems worldwide.[5] Understanding the risk factors underlying hyperlipidemia has significant public health implications for disease prevention.

Tooth loss is the final consequence of prevalent oral diseases like periodontitis and caries, both of which are considered as oral bacterial infections that give rise to inflammatory processes in the oral cavity.[6,7] Previous studies have shown that the cumulative oral inflammation promotes systemic inflammation level.[8] There is compelling evidence that periodontitis raises the burden of cumulative systemic inflammation and adds to cardiovascular disease risk factors.[9–11] Moreover, Streptococcus mutans (S. mutans), which is widely recognized as the primary causative pathogen for dental caries, has been identified in atheromatous plaque specimens[12] and cardiovascular specimens,[13] suggesting a potential association with CVD.

The cumulative inflammatory status of oral health, as indicated by the number of missing teeth, is widely recognized as a crucial factor in assessing overall oral health.[14,15] Self-reported count of absent teeth has previously been validated as reliable indicator for assessing oral health in large-scale population surveys.[16] The presence of multiple missing teeth

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can suggest that the individual has a history of periodontitis.[14] The association between periodontitis and inflammation is well-established and supported by extensive scientific evidence.[17,18] The systemic inflammation is thought to be a result of the chronic inflammatory burden imposed by periodontal disease. Tooth loss may then reflect the past inflammatory and infectious state of oral health.[15]

Several studies suggest a link between oral health, specifically tooth loss, and CVD.[19–21] Subjects with missing teeth were more likely to suffer from metabolic syndrome (MetS), whereas dyslipidemia is a key component of MetS. These lipid metabolism abnormalities are a major risk factor for CVD. In addition, a recent systematic review also documented that periodontitis was linked to hyperlipidemia in humans.[22] All these data imply that the number of missing teeth may also be related to hyperlipidemia, mediated by systemic chronic inflammation. Despite previous findings, no long-term prospective cohort investigations have reported the correlation between the number of missing teeth and hyperlipidemia within the general adult population of China.

Therefore, this research premise aimed to explore if the baseline number of missing teeth was linked to the incidence of hyperlipidemia in a prospective cohort investigation in the Chinese general adult population.

Methods

Study Design and Sample

The cohort examined in this analysis consisted of individuals belonging to the Tianjin Chronic Low-Grade Systemic Inflammation and Health (TCLSIH) cohort. This particular study, TCLSIH cohort, is an ongoing and prospective investigation into dynamic cohort trends. The cohort was established in August 2012 and officially launched in May 2013. Participants were selected from multiple hospitals' affiliated health examination centers (or health management centers), urban/suburban/rural communities, and different levels of nursing homes that agreed to participate in the survey.

The inclusion criteria for this study consisted of adults aged 18 years and above who had been residents of Tianjin for a minimum of 5 years. The study randomly selected adults who underwent annual medical health examinations (including routine health checks such as height, weight, waist circumference, blood pressure, blood routine, blood biochemistry, etc.) to complete a structured lifestyle questionnaire at baseline. Participants who had undergone health examinations, such as a blood test, were recruited for the study and given a detailed questionnaire about tooth loss, smoking and drinking habits, disease history, education, physical activity, socioeconomic status, lifestyle factors, as well as dietary intake. The cohort achieved an overall response rate of 97.1%, excluding individuals with disabilities, severe mental illness, severe cognitive impairment, hearing impairment, pregnancy, and other factors.

The implementation of this investigation adheres to the principles stated in the Helsinki Declaration, with all participants explicitly granting their consent through written informed documentation. The TCLSIH cohort study obtained approval from the Ethics Committee of Tianjin Medical University (No.: TMUhMEC201430).

Our study included 20,155 participants initially. The exclusion criteria were as follows: (1) invalid questionnaires (n = 959), (2) baseline hyperlipidemia (n = 2135), (3) a history of cardiovascular disease (n = 837), (4) a history of cancer (n = 167), and people taking lipid-lowering agents (n = 403). In addition, we further exclude those failure to follow up during the study (n = 1722, follow-up rate = 89.0%). Following the application of the criteria for participation, there were a total of 13,932 participants who participated in the final cohort analyses. A flowchart is shown in Figure 1.

Determination of the Number of Missing Teeth

In the survey, participants were asked to recall and document the number of teeth they were missing (excluding wisdom teeth). For those who had difficulty remembering, healthcare professionals provided assistance during the examination. In accordance with the National Health and Nutrition Survey's findings on adult tooth loss, the average number of permanent teeth among individuals aged 20 to 64 was 24.9 teeth.[23] Consequently, we categorized the number of missing teeth into three groups: 0, 1–2, and ≥3. The first group, consisting of individuals with 0 missing teeth, represents subjects with periodontal health (controls). The second group, with 1 to 2 missing teeth, is likely attributed to localized periodontal or caries disease affecting individual teeth. Individuals missing ≥3 teeth may have experienced long-term moderate chronic periodontitis or other minor reasons leading to additional tooth loss.

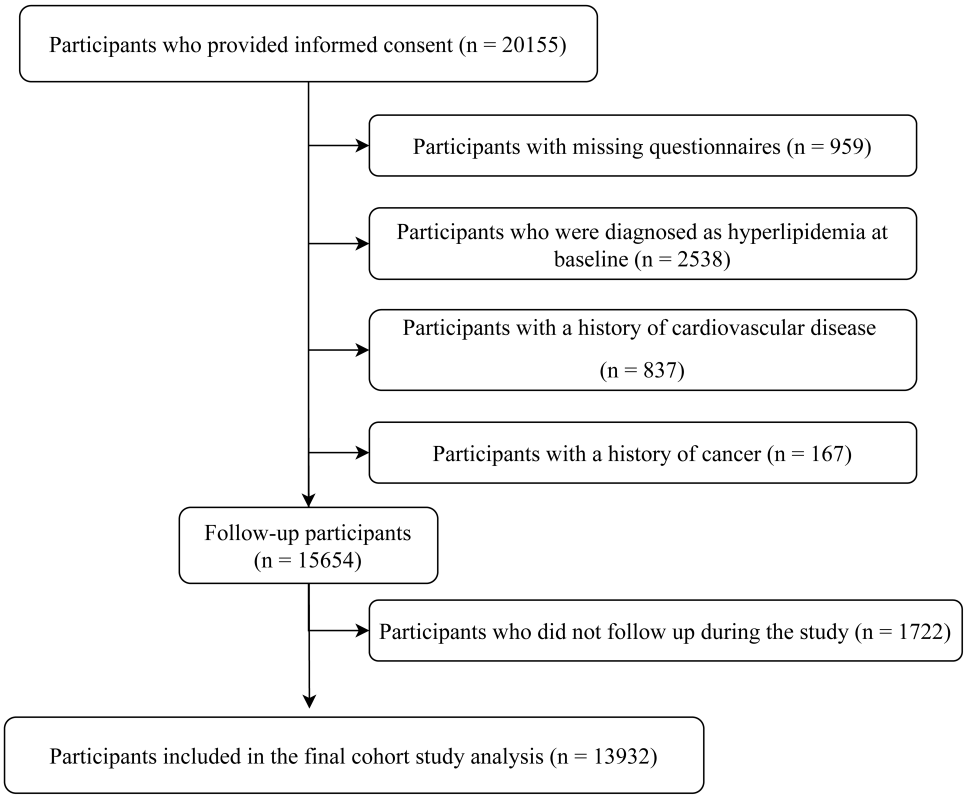

Figure 1 Flow diagram showing the selection of the study population.

Assessment of Hyperlipidemia

The definition of hyperlipidemia was determined by considering the onset date as the midpoint between the last checkup where the values were within normal range and the checkup date, which was based on the results obtained from analyzing fasting blood samples. These blood samples were drawn from the antecubital area after an overnight fast of 8–12 hours and collected in silicone-coated vacuum plastic tubes for the purpose of analyzing blood lipid levels. The enzymatic methods were used to assess the levels of triglycerides (TG) and total cholesterol (TC), while the precipitation method involving polyvinyl sulfuric acid was employed to measure LDL cholesterol (LDL-C), and the chemical precipitation method was used to determine HDL cholesterol (HDL-C). Hyperlipidemia was defined as TG levels equal to or above 1.7 mmol/L, TC levels equal to or above 5.17 mmol/L, LDL-C levels equal to or above 3.37 mmol/L, or a self-reported diagnosis of hyperlipidemia by a physician during follow-up visits.[24]

Assessment of Other Variables

Demographic factors (gender, education level, employment status, age, and income level), level of physical activity, family medical history, smoking habits, and personal medical records were obtained via completion of a comprehensive questionnaire.[25] Trained professionals adhering to standardized protocols carried out the measurement and recording of participants' height and weight. Body mass index (BMI) was computed by dividing weight (in kilograms) by the square of height (in meters), providing a measure of overall body composition. Waist circumference (WC) was assessed using a measuring tape placed near the navel, while participants stood upright and breathed normally (in centimeters). To evaluate dietary habits, a modified version of the food frequency questionnaire (FFQ) was employed. Lastly, physical activity levels during the previous week were assessed utilizing the International Physical Activity Questionnaire (IPAQ).

Serum fasting blood glucose (FBG) contents were determined via the glucose oxidase approach. Type 2 diabetes was defined according to the World Health Organization[26] as a fasting blood glucose level of ≥ 7 mmol/L or a history of diabetes. Blood pressure was measured using an electronic blood pressure monitor (TM-2655, A&D Company, Japan). Before measuring blood pressure, participants were asked to rest for five minutes and then position their right upper arm at heart level to begin the

measurement. The average of two measurements was taken as the final recorded blood pressure value. If the systolic blood pressure was ≥140 mmHg, the diastolic blood pressure was ≥90 mmHg or the participant self-reported a history of hypertension, it was defined as having hypertension. All protocols were completed in the same environment to address potential sources of bias.

Statistical Analysis

Statistical analyses were conducted using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA). Geometric means (95% CI) are used to present continuous variables, while percentages are used to present categorical variables. The number of missing teeth was considered the independent variable, whilst hyperlipidemia incidence was the dependent variable. Calculation of the follow-up time was done from the date of completion of the baseline FFQ survey to the date of the first diagnosis of hyperlipidemia, the end of follow-up (December 31, 2019), or loss to follow-up, whichever was earliest. Due to significant differences in the prevalence of hyperlipidemia between males and females, we conducted a stratified analysis by gender. We adopted four Cox proportional-hazards regression models to determine the relationship between the number of missing teeth with hyperlipidemia risk. Model 1 was a crude model. In model 2, we adjusted only for age and BMI, and in model 3, we additionally adjusted for smoking status, family history of disease (including cardiovascular disease, hypertension, hyperlipidemia, and diabetes), drinking status, hypertension, diabetes, education level, depressive symptoms, working status, healthy pattern score, total energy intake, household income, physical activity, sweet pattern score, and animal pattern score. Model 4 was additionally adjusted for the baseline values of serum lipids including LDL, TG, and HDL. The linear trend test was determined by including the categories of tooth loss (0, 1–2, and ≥3) as continuous variables in the model. The hazard ratios and 95% CIs were determined. Two-tailed p-values were used for all statistical tests, and a significance level of $P < 0.05$ was considered statistically significant.

Results

Baseline Characteristic of Participants

From May 2013 to December 2019, a total of 13,932 subjects ultimately completed the study. Tables 1 and 2 display the statistics of the male and female participants at baseline, respectively. In this cohort study, 49.6% (6914 of 13,932) of participants were male, and 50.4% (7018 of 13,932) were female. Male participants with more missing teeth were older; had higher BMI, LDL-C, WC, SBP, TC, TG, FBG, DBP, as well as physical activity (PA); consumed more alcohol ("every day"); exhibited higher smoking status rates ("current smoker", "ex-smoker"); and had diabetes as well as a family history of cardiovascular and hypertension but had lower total energy intake, healthy intake, education level, or

Table 1 Baseline Characteristics of Participants According to the Number of Missing Teeth in Male (n=6914)[a]

Characteristics	The Number of Missing Teeth			*P* for Trend[b]	*P* value[c]
	0	1–2	≥3		
No. of participants	4362	1529	1023	–	–
Age (years)	34.4 (29.5, 42.6)	43.6 (34.7, 51.9)	54.0 (45.2, 62.7)	<0.0001	<0.0001
BMI (kg/m^2)	24.8 (22.7, 27.2)	25.1 (22.6, 27.3)	25.1 (23.2, 27.3)	0.01	0.04
WC (cm)	86.0 (80.0, 92.0)	87.0 (80.0, 93.0)	89 (82, 94)	<0.0001	<0.0001
TC (mmol/L)	4.35 (3.91, 4.76)	4.46 (4.04, 4.84)	4.45 (4.00, 4.87)	<0.0001	<0.0001
TG (mmol/L)	1.04 (0.78, 1.38)	1.09 (0.83, 1.46)	1.12 (0.83, 1.43)	<0.001	<0.0001
LDL-C (mmol/L)	2.56 (2.16, 2.94)	2.62 (2.23, 2.99)	2.63 (2.23, 3.00)	<0.001	<0.0001
HDL-C (mmol/L)	1.24 (1.08, 1.44)	1.26 (1.10, 1.47)	1.25 (1.07, 1.47)	0.10	0.01
SBP (mmHg)	120 (110, 130)	120 (110, 130)	125 (115, 135)	<0.0001	<0.0001
DBP (mmHg)	75 (70, 80)	80 (70, 85)	80 (70, 85)	<0.0001	<0.0001
FBG (mmol/L)	5.00 (4.70, 5.30)	5.00 (4.80, 5.40)	5.20 (4.90, 5.70)	<0.0001	<0.0001
Physical activity (Mets × hr/week)	13.8 (5.50, 28.5)	15.1 (5.78, 29.4)	16.5 (6.44, 34.7)	0.04	0.13
Total energy intake (kcal/day)	2437.5 (1852, 3149.4)	2408.8 (1847.8, 3099.2)	2344.4 (1735.2, 3039.4)	0.02	0.02
Sweet pattern score	−0.24 (−0.56, 0.23)	−0.20 (−0.51, 0.27)	−0.23 (−0.57, 0.30)	0.92	0.90
Healthy pattern score	−0.02 (−0.27, 0.35)	−0.04 (−0.35, 0.32)	−0.1 (−0.43, 0.26)	<0.001	<0.01
Animal pattern score	0.02 (−0.48, 0.60)	0.04 (−0.50, 0.63)	0.04 (−0.51, 0.63)	0.98	0.95

(*Continued*)

Table 1 (Continued).

Characteristics	The Number of Missing Teeth			*P* for Trend[b]	*P* value[c]
	0	1–2	≥3		
Depressive symptoms (%)	573 (14.98)	212 (16.41)	133 (16.16)	0.24	0.24
Smoking status (%)					
Current smoker	1142 (28.9)	476 (33.64)	383 (39.69)	<0.0001	<0.0001
Ex-smoker	296 (7.49)	142 (10.04)	149 (15.44)	<0.0001	<0.0001
Non-smoker	2514 (63.61)	797 (56.33)	433 (44.87)	<0.0001	<0.0001
Drinking status (%)					
Everyday drinker	154 (4.03)	82 (5.93)	122 (12.99)	<0.0001	<0.0001
Sometime drinker	2853 (74.59)	1019 (73.68)	574 (61.13)	<0.0001	<0.0001
Ex-drinker	398 (10.41)	127 (9.18)	99 (10.54)	0.73	0.73
Non-drinker	420 (10.98)	155 (11.21)	144 (15.34)	0.01	0.01
Education level (≥College graduate, %)	3659 (84.27)	1133 (74.54)	537 (53.06)	<0.0001	<0.0001
Working status (%)					
Managers	2099 (53.38)	753 (53.29)	424 (44.07)	<0.0001	<0.0001
Professionals	832 (21.16)	283 (20.03)	149 (15.49)	0.001	0.001
Other	1001 (25.46)	377 (26.68)	389 (40.44)	<0.0001	<0.0001
Household income (≥10,000 Yuan, %)	1863 (43.55)	645 (42.94)	290 (28.97)	<0.0001	<0.0001
Diabetes (yes, %)	124 (2.84)	108 (7.06)	147 (14.40)	<0.0001	<0.0001
Family history of disease (%)					
CVD	1044 (26.29)	453 (31.79)	356 (36.63)	<0.0001	<0.0001
Hypertension	1905 (47.97)	749 (52.56)	521 (53.6)	0.001	0.001
Hyperlipidemia	15 (0.38)	4 (0.28)	2 (0.21)	0.37	0.37
Diabetes	940 (23.67)	351 (24.63)	235 (24.18)	0.59	0.59

Notes: [a]Continuous variables are expressed as medians (P25, P75) and categorical variables are expressed as numbers (percentages). [b]*P* for trend is based on general linear models or logistic regression models. [c]*P* value for the comparison among the three groups.

Abbreviations: BMI, body mass index; WC, waist circumference; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; CVD, cardiovascular disease.

Table 2 Baseline Characteristics of Participants According to the Number of Missing Teeth in Females (n=7018)[a]

Characteristics	The Number of Missing Teeth			*P* for Trend[b]	*P* value[c]
	0	1–2	≥3		
No. of participants	4845	1461	712	–	–
Age (years)	34.3 (29.5, 41.0)	40.2 (33.3, 46.5)	46.8 (38.3, 54.1)	<0.0001	<0.0001
BMI (kg/m^2)	21.7 (20.0, 23.9)	22.4 (20.6, 24.5)	22.7 (20.7, 24.9)	<0.0001	<0.0001
WC (cm)	73 (68, 79)	74 (69, 81)	76 (70, 82)	<0.0001	<0.0001
TC (mmol/L)	4.3 (3.86, 4.71)	4.39 (3.95, 4.81)	4.49 (4.08, 4.91)	<0.0001	<0.0001
TG (mmol/L)	0.76 (0.59, 0.99)	0.80 (0.63, 1.05)	0.88 (0.67, 1.17)	<0.0001	<0.0001
LDL-C (mmol/L)	2.33 (1.95, 2.72)	2.41 (2.04, 2.77)	2.47 (2.09, 2.83)	<0.0001	<0.0001
HDL-C (mmol/L)	1.54 (1.33, 1.79)	1.54 (1.32, 1.79)	1.52 (1.31, 1.8)	0.65	0.90
SBP (mmHg)	110 (100, 120)	110 (105, 120)	115 (105, 130)	<0.0001	<0.0001
DBP (mmHg)	70 (65, 75)	70 (65, 75)	70 (65, 80)	<0.0001	<0.0001
FBG (mmol/L)	4.80 (4.60, 5.10)	4.80 (4.60, 5.10)	4.90 (4.60, 5.20)	<0.0001	<0.0001
Physical activity (Mets × hr/week)	9.90 (3.30, 20.58)	9.90 (3.30, 20.33)	11.6 (3.53, 23.9)	0.04	0.12
Total energy intake (kcal/day)	2070.4 (1570, 2690.8)	2092.3 (1565.9, 2693.4)	2149.9 (1605.2, 2805.3)	0.39	0.69
Sweet pattern score	−0.09 (−0.44, 0.32)	−0.03 (−0.40, 0.40)	−0.07 (−0.48, 0.42)	0.91	0.14
Healthy pattern score	−0.19 (−0.45, 0.03)	−0.24 (−0.51, 0.01)	−0.23 (−0.53, 0.00)	0.03	0.06
Animal pattern score	−0.21 (−0.63, 0.29)	−0.22 (−0.66, 0.32)	−0.14 (−0.59, 0.38)	0.86	0.98
Depressive symptoms (%)	672 (16.35)	214 (17.89)	95 (17.50)	0.25	

(*Continued*)

Table 2 (Continued).

Characteristics	The Number of Missing Teeth			*P* for Trend[b]	*P* value[c]
	0	1–2	≥3		
Smoking status (%)					
Current smoker	32 (0.73)	13 (0.96)	14 (2.11)	0.01	0.01
Ex-smoker	23 (0.52)	11 (0.81)	2 (0.30)	0.98	0.98
Non-smoker	4328 (98.75)	1328 (98.22)	648 (97.59)	0.01	0.01
Drinking status (%)					
Everyday drinker	23 (0.54)	10 (0.76)	6 (0.94)	0.17	0.17
Sometime drinker	1720 (40.36)	557 (42.42)	256 (40.00)	0.64	0.64
Ex-drinker	403 (9.46)	126 (9.60)	41 (6.41)	0.051	0.051
Non-drinker	2116 (49.65)	620 (47.22)	337 (52.66)	0.65	0.65
Education level (≥College graduate, %)	4057 (84.12)	1077 (74.12)	399 (56.36)	<0.0001	<0.0001
Working status (%)					
Managers	2384 (54.62)	691 (51.19)	296 (44.58)	<0.0001	<0.0001
Professionals	579 (13.26)	186 (13.78)	84 (12.65)	0.89	0.89
Other	1402 (32.12)	473 (35.04)	284 (42.77)	<0.0001	<0.0001
Household income (≥10,000 Yuan, %)	2215 (46.53)	582 (40.61)	228 (33.00)	<0.0001	<0.0001
Diabetes (yes, %)	44 (0.91)	39 (2.67)	21 (2.95)	<0.0001	<0.0001
Family history of disease (%)					
CVD	1289 (29.08)	483 (35.51)	257 (38.30)	<0.0001	<0.0001
Hypertension	2256 (50.89)	762 (56.03)	375 (55.89)	0.001	0.001
Hyperlipidemia	15 (0.34)	7 (0.51)	4 (0.60)	0.23	0.23
Diabetes	1229 (27.72)	404 (29.71)	170 (25.34)	0.69	0.69

Notes: [a]Continuous variables are expressed as medians (P25, P75) and categorical variables are expressed as numbers (percentages). [b]*P* for trend is based on general linear models or logistic regression models. [c]*P* value for the comparison among the three groups.
Abbreviations: BMI, body mass index; WC, waist circumference; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; CVD, cardiovascular disease.

household income. Furthermore, female participants with more missing teeth were older; harbored higher LDL-C, DBP, WC, TC, BMI, TG, SBP, FBG, and PA; harbored higher smoking status rates ("current smoker"); and had diabetes as well as a family history of cardiovascular and hypertension but lower healthy intake, education level, as well as household income. Other indicators were not remarkably different.

Relationship of the Number of Missing Teeth with Hyperlipidemia

During a median follow-up of 4.2 years (range, 1.0–6.0 years), we identified 6756 incident hyperlipidemia cases during 42,048 person-years of follow-up. Table 3 provides the relationship of the number of missing teeth with hyperlipidemia after adjusting for confounding factors. In model 3, the multivariable hazard ratios (95% CI) of hyperlipidemia across the categories of missing teeth were as follows: in male participants, 1.00 (reference), 1.04 (0.96, 1.13), and 1.01 (0.91, 1.11) (*P* for trend = 0.63); in female participants, 1.00 (reference), 1.08 (0.99, 1.18), and 1.23 (1.09, 1.38) (*P* for trend < 0.001), respectively. In model 4, the results showed that the association between the number of missing teeth and hyperlipidemia remained in females, but the effect size was weakened from 23% to 18% after adjusting for baseline blood lipid levels. There was a remarkable connection between the number of missing teeth and hyperlipidemia only in female participants. *P* for the trend test across the three categories (0, 1–2, and ≥3) was significant.

Discussion

After adjusting for potential confounders, female subjects who had ≥3 missing teeth had an 18% increased risk of hyperlipidemia, in comparison with those with no missing teeth. The primary finding of this prospective cohort study is an association between the incidence of hyperlipidemia and the number of missing teeth in females.

It is reported that the missing teeth and periodontal disease may increase the rate of prevalence of several chronic noncommunicable diseases.[27] Accumulated evidence has indicated a correlation between the number of missing teeth

Table 3 Adjusted Hazard Ratios (95% Confidence Intervals) for Associations of the Number of Missing Teeth with the Incidence of Hyperlipidemia

	The Number of Missing Teeth			P for Trend[a]
	0	1–2	≥3	
Male				
No. of participants	4362	1529	1023	-
No. of hyperlipidemia	2358	865	585	-
Person years	10,074.5	3429.5	2340.5	-
Incidence per 1000 person-years	234	252	250	-
Model 1[b]	1.00 (reference)	1.08 (0.99, 1.16)[c]	1.07 (0.98, 1.17)	0.07
Model 2[d]	1.00 (reference)	1.07 (0.99, 1.16)	1.06 (0.96, 1.17)	0.13
Model 3[e]	1.00 (reference)	1.04 (0.96, 1.13)	1.01 (0.91, 1.11)	0.63
Model 4[f]	1.00 (reference)	1.10 (0.98, 1.22)	1.03 (0.91, 1.16)	0.30
Female				
No. of participants	4845	1461	712	-
No. of hyperlipidemia	1917	655	376	-
Person years	12,321.0	3628.5	1635.5	-
Incidence per 1000 person-years	156	181	230	-
Model1[b]	1.00 (reference)	1.16 (1.06, 1.27)[3]	1.48 (1.33, 1.66)	<0.0001
Model2[d]	1.00 (reference)	1.11 (1.02, 1.22)	1.29 (1.14, 1.45)	<0.0001
Model3[e]	1.00 (reference)	1.08 (0.99, 1.18)	1.23 (1.09, 1.38)	<0.001
Model4[f]	1.00 (reference)	1.09 (0.99, 1.19)	1.18 (1.04, 1.33)	<0.01

Notes: [a]Cox regression analysis. [b]Crude model. [c]Hazard ratios (95% confidence interval) (all such values). [d]Adjusted for age and body mass index. [e]Adjusted for age, BMI, smoking status, drinking status, family history of disease (including cardiovascular disease, hypertension, hyperlipidemia, and diabetes), hypertension, diabetes, education level, working status, household income, physical activity, depressive symptoms, total energy intake, sweet pattern score, healthy pattern score, animal pattern score. [f]Additionally adjusted for the baseline values of serum lipids including LDL, TG, and HDL.

and various CVD.[19,20,28,29] Meanwhile, periodontitis is associated with abnormal lipid profiles.[30,31] Meanwhile, studies have also found that women harboring low contents of HDL cholesterol had a remarkably higher risk of periodontitis[32] and that high serum total cholesterol was linked with periodontitis.[33] As an important measure for oral health, a national cohort investigation also showed that frequent brushing of teeth could reduce blood TG contents and increase HDL-C contents.[34] Our study has contributed to the existing body of evidence in this field, enhancing both the content and strength of the evidence to a certain degree.

The number of missing teeth is often used as a surrogate marker of periodontitis for some studies.[14] Numerous studies have investigated the relationship between the number of missing teeth and periodontitis. The association between periodontitis and inflammation is well-established and supported by extensive scientific evidence. Hence, the number of missing teeth may then reflect the past inflammatory and infectious state of oral health.[35]

The potential mechanisms and biological foundations of this association may be as follows. First, chronic oral infections such as periodontitis and dental caries often lead to tooth loss which can trigger systemic low-grade inflammation, as well as insulin resistance. This inflammation may disrupt and affect lipid metabolism, leading to increased lipid levels in the blood. Second, the oral microbiome is strongly associated with the gut microbiome. The loss of teeth can alter the composition of the oral microbiota, which may subsequently impact the gut microbiota. Several studies have suggested that dysbiosis of the gut microbiota may affect lipid metabolism, resulting in the development of hyperlipidemia.[36] Third, tooth loss can have an impact on an individual's dietary habits. Difficulties with chewing and oral discomfort resulting from tooth loss can limit food choices and intake, leading to an imbalanced diet that is high in fat, sugar, and cholesterol. This can increase the risk of hyperlipidemia.[37] Fourth, both tooth loss and hyperlipidemia may be influenced by socioeconomic factors. Individuals from lower socioeconomic backgrounds may have poorer access to dental care and a higher likelihood of consuming a diet high in unhealthy fats, both of which could contribute to tooth loss and hyperlipidemia. The socioeconomic status differences and hormonal level disparities in gender could potentially explain the relationship between tooth loss and hyperlipidemia in part. Further study is required to elucidate these

potential mechanisms and to understand the extent to which they contribute to the association between missing teeth and hyperlipidemia.

The strengths of this study are the use of longitudinal data and the long-term cohort study, with a higher level of evidence, we adjusted for many confounders, with evidence suggesting a causal relationship to some extent, which has rarely been reported in previous studies. In addition, this study directly explored the relationship between missing teeth and hyperlipidemia in the large Chinese adult population. Such information could inform strategies for preventing and managing both conditions, potentially improving cardiovascular health outcomes.

A limitation of this research work was that the number of missing teeth was recalled by participants and the reasons for tooth loss were not recorded, making it more subjective and prone to recall bias. The number of missing teeth was assessed once at baseline, therefore, the changes in the number of missing teeth over time were not considered. Future research warrants investigating the association with repeated measures data. Finally, it cannot establish a causal relationship and the likelihood of residual confounding may remain.

Conclusion

The number of missing teeth was independently associated with the incidence of hyperlipidemia in females. Therefore, incorporating oral health maintenance into primary prevention of hyperlipidemia holds significant public health significance.

Data Sharing Statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The research protocol was granted approval by the Institutional Review Board of Tianjin Medical University (No: TMUhMEC201430), and all subjects participated voluntarily in the research work and provided written informed consent.

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Disclosure

The authors report no conflicts of interest in this work.

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