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Liver and Kidney Disease and Periodontal Disease: A Cross-sectional Study Based on Data from Oral Health Branch of Rafsanjan Cohort Study

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Abstract

Objectives: Several studies suggest that periodontal disease may be associated with some systemic disease, including liver and kidney disease. This research aimed to investigate the potential relationship between liver and kidney disease and periodontal disease.

Methods: The study conducted a cross-sectional analysis on 8,682 individuals aged 35-70 who were registered with the Oral Health Branch of Rafsanjan Cohort Study (OHBRCS). OHBRCS is part of the Rafsanjan Cohort Study (RCS) and the larger Prospective Epidemiological Research Studies in IRAN (PERSIAN) initiative which began in 2015 in Rafsanjan, in southeastern Iran. After applying the inclusion and exclusion criteria, the final study population consisted of 6545 participants. To investigate liver disease, liver enzymes including Alanine Transaminase (ALT), Aspartate Transaminase (AST), Alkaline Phosphatase (ALP) and Gamma-Glutamyltransferase (GGT) were investigated. Hematuria and proteinuria and Glumerular Filtration (GFR) were used to check the kidney disease. In order to investigate periodontal disease,all subjects were examined by dental specialists in terms of gum health parameters, including bleeding during probing or BOP, gingival erosion or CAL, pocket depth of the probe or the presence of dental calculus. Univariate and multivariate logistic regression analyses were performed to analyze the data.

Results: No significant association was found between liver and kidney disease indexes and periodontal disease indexes.

Conclusion: Overall, this study suggests that there was no significant association between liver and kidney disease and periodontal disease.

Keywords: Periodontal disease; Liver disease; Kidney disease; Rafsanjan Cohort Study (RCS); Prospective Epidemiological Research Studies in IRAN (PERSIAN)

Introduction

Periodontal disease, characterized by the loss of bone and inflammation around the teeth, is a prevalent oral disease that often leads to tooth loss in older individuals. The clinical diagnosis of periodontal disease involves identifying signs and symptoms such as bleeding during probing, pocket depth and clinical attachment loss. This condition can be prevented by practicing good dental hygiene, reducing risk factors, making lifestyle modifications, undergoing regular periodontal check-ups, and controlling dental plaque [1].

Currently, the treatment of periodontitis aims to alleviate adverse clinical manifestations.

Chronic periodontitis, the most common form of the disease, can range in severity from mild to severe. The severe form affects approximately 11 percent of the global population, with its prevalence increasing with age until around 50-60 years old. Various factors, including age, socioeconomic status, education level, smoking, stress, and systemic diseases, influence the development and progression of this slowly advancing condition [2].

Periodontal diseases have been linked to several significant acute and chronic systemic diseases.

Numerous studies, both in animals and humans, have established a connection between periodontitis and non-alcoholic fatty liver disease. Liver diseases, such as non-alcoholic fatty liver disease, liver cirrhosis, liver cancer, and other forms of liver damage, are substantial health concerns worldwide. Non-Alcoholic Fatty Liver Disease (NAFLD) is presently the most prevalent liver disease globally, affecting about 25.2 percent of adults aged 18 or above. The prevalence of NAFLD is rising globally, in parallel with increasing rates of obesity, metabolic syndrome, and diabetes, making it a significant global health issue. Additionally, NAFLD increases the risk of liver cirrhosis, end stage liver disease, hepatocellular carcinoma, and mortality. The release of toxins and pro-inflammatory cytokines during periodontal inflammation can easily enter the bloodstream, reach the liver tissue, and contribute to lipid peroxidation, oxidative stress, and the progression of liver disease.

Chronic kidney disease and chronic periodontitis are both common conditions that are disproportionately associated with each other. It has been reported that the progression of one disease can impact the other. Furthermore, these conditions share risk factors and have a common source of systemic

inflammation. Chronic Kidney Disease (CKD) is a significant global health issue with a high prevalence, significantly affecting the overall health and quality of life of patients. CKD is defined as kidney damage, such as proteinuria, hematuria, or decreased kidney function (Glomerular Filtration Rate (eGFR) <60 mL/min/1.73 m² for >3 months). In the active stages of periodontitis, the production of inflammatory cytokines can increase the levels of C-reactive proteins, which contribute to the development of CKD [3].

Investigating the acccosiation between liver and kidney disease and periodontal disease is essential given the possible relationship of liver and kidney disease and periodontal health. Within the adult population of the Oral Health Branch of Rafsanjan Cohort Study (OHBRCS), we want to examine the relationship between liver and kidney diseases and periodontal disease in this paper.

Materials and Methods

Study design

In order to investigate the potential relationship liver and kidney disease and periodontal diseases in people aged 35 to 70 who were registered at the Oral Health Branch of the Rafsanjan Cohort Study (OHBRCS), this study was authorized by the ethics committee of Rafsanjan University of Medical Sciences (Ethical codes: ID: IR.RUMS.REC.1402.060). OHBRCS is a component of the Rafsanjan Cohort Study (RCS). RCS, which is a component of Prospective Epidemiological Research Studies in Iran (Persian), began operations in Rafsanjan in 2015 [4].

8682 people took part in OHBRCS. The participants were interviewed using a validated, organized, and complete questionnaire that included questions on socioeconomic status, personal habits, medical history, and demographic and anthropometric data.

The criteria for entering this study include the following:

- Age 35 to 70 years.
- All people must have been included in the Rafsanjan cohort study.
- To live only in the designated area.
- Be Iranian (have a national card or birth certificate).
- Be a resident of this city for at least nine months a year.
- The presence of at least 2 teeth.

The study excluded people who were pregnant and those who were using dietary supplements. 6545 persons made up the study's final population after the inclusion and exclusion criteria were applied.

Liver and kidney health assessment

Fasting blood samples and urine samples were collected from all research participants and biochemical parameters were checked using a Biotecnica autoanalyzer (BT 1500, Italy) in the central laboratory of the cohort. In this study, liver enzymes including Alanine Transaminase (ALT), Aspartate Transaminase (AST), Alkaline Phosphatase (ALP), and Gamma-Glutamyltransferase (GGT) were investigated. Hematuria, proteinuria and Glomerular Filtration (GFR) were used to check kidney health parameters

Hematuria: The presence of ≤ 3 RBC in urine

Proteinuria: The presence of protein ≥ 1+ in the urine

GFR reduction: GFR<60 mL/min/1.73 m^2

Elevated ALT: ≥ 35 U/L in women and ≥ 40 U/L in men

Elevated AST: ≥ 35 U/L in women and ≥ 40 U/L in men

Elevated ALP: ≥ 306 U/L in both sexes

Increased GGT: ≥ 37 U/L in women and ≥ 54 in men

Periodontal health assessment

Indicators of gingival health, such as BOP, Clinical Attachment Loss (CAL), Periodontal Probing Depth (PPD), and dental calculus, were assessed in all patients. A qualified dentist examined the patients on a dental unit while utilizing a disposable dental mirror and a Williams probe (Michigan "o" probe williams coded, Hu-Friedy, USA) to record the gingival indices. Each tooth had four spots that were gently probed in order to calculate the BOP index. After 30 to 60 seconds, the presence or absence of bleeding was noted. The ratio of bleeding points to all points is known as the BOP index for each individual.

To measure CAL, the area around the teeth was thoroughly probed, and the distance between the CEJ and the depth of the pocket was noted. This analysis determined only plaque-induced CAL. The probe was moved parallel to the axis of the teeth along the gingival margin to measure the pocket depth, which is the vertical distance from the free gingival margin to which a probe penetrates into a pocket. The deepest entrance points of the probe in six sides (mesial, middle, and distal of buccal and lingual surfaces) were recorded. In this investigation, only real pockets were counted. Dental calculus was evaluated using the CSI (Calculus Surfce Index) index; in this manner, the four surfaces of buccal, lingual, mesial and distal of the four front teeth of the mandible were assessed by observation or touch with a probe [5].

Other variables assessment

The Wealth Score Index (WSI) was used to check the state of well-being. Multiple Correspondence Analysis (MCA) was used to calculate the Wealth Score Index (WSI), which was then used to evaluate the socioeconomic standing of the individuals. The WSI for each participant was determined by factoring in their possession of a variety of durable items (such as a dishwasher, car, and TV), the condition of their home (such as the number of rooms and kind of ownership), and their level of education [6].

The amount of physical activity was evaluated using the Metabolic Equivalent of Task (MET). Through the completion of a questionnaire, the individuals' daily activities were recorded for the study. For this, the Metabolic Equivalent of Task (MET) criteria was employed. The quantity of energy spent by each person in relation to their weight is represented by a MET. As an

illustration, one MET is equal to 3.5 mL of oxygen used per kilogram of body weight per minute by each person at rest, whereas four METs is equal to 16 ml of oxygen used per kilogram of body weight per minute. We evaluated each participant's activity levels using MET.

Dyslipidemia is defined as having either LDL levels greater than or equal to 130 mg/dL, total cholesterol levels greater than or equal to 200 mg/dL, HDL levels less than or equal to 40 mg/dL in males and 50 mg/dL in females, or triglyceride levels greater than or equal to 150 mg/dL. Additionally, if someone has taken medication to lower their lipid levels within the past two weeks, they are also considered to have dyslipidemia [7].

Statistics analysis

Following collection, data were processed in a STATA 14 environment, and the findings were shown through the use of tables and descriptive statistical techniques. With the use of the *chi-square* test (2) for categorical variables and the t-test for quantitative variables, the basic characteristics of the analyzed groups were compared. For categorical data, number and percentage (%) were used, and for quantitative variables, mean (SD: Standard Deviation). To reduce the impact of confounding factors, the analysis was conducted in two stages using a univariate and multivariate logistic regression model. The factors that emerged as significant in the univariate phase of the multivariate analysis were included to the multivariable logistic regression model, and the odds ratio was determined as a result. Age (continuous variable), gender (male/female), education (continuous variable), wealth status index (continuous variable), smoking (yes/no), opium use (yes/no), body mass index (yes/no), activity level (yes/no), hypertension (yes/no), diabetes (yes/no), history of CVD (yes/no), and brushing (yes/no) were adjusted in the model. The thresholds for significance was set at values lower than 0.05 [8].

Results

This study involved 6545 participants with an average age of 47.61 years and a standard deviation of 8.74 years. Of these participants, 44.20% were men and 55.80% were women. The prevalence of BOP (Bleeding on Probing), calculus, pocket depth and Clinical Attachment Loss (CAL) was found to be 73.51%, 81.56%, 13.72%, and 59.67%, respectively, among this population. Also, the prevalence of ALT, AST, ALP, and GGT enzymes were 9.72%, 2.78%, 8.16%, and 9.16%, respectively. The prevalence of decreased GFR, hematuria and proteinuria were 12.79%, 17.97% and 4.29%, respectively [9].

Table 1 shows sociodemographic characteristics, personal habits and medical history of the study population by ALT and AST. The frequency of ALT elevate was significantly higher in men (P-value<0.001) and people who consumpted alcohol (P-value<0.001) and had a history of diabetes (P-value 0.012) and dyslipidemia (P-value<0.001). Individuals with elevated ALT had significantly higher mean of education (P-value 0.003), age (P-value<0.001) and BMI (P-value<0.001), and also had less tooth brushing frequency (P-value<0.001) [10].

People with elevated AST had significantly more frequency of hypertension (P-value 0.002), diabetes (P-value 0.010) and dyslipidemia (P-value<0.001). Individuals with elevated AST had significantly lower mean physical activity (P-value 0.007) and higher BMI (P-value<0.001) [11].

Table 1: Sociodemographic characteristics, personal habits and medical history of the study population by ALT and AST (n=6545).

Characteristics	Overall (n=6545)	Elevated ALT		P-Value	Elevated AST		P-Value
		No (n=5909)	Yes (n=636)		No (n=6363)	Yes (n=182)	
Age-year-no (%)				<0.001			0.587
35-45	3004 (45.90)	2643 (44.73)	361 (56.76)		2915 (45.81)	89 (48.90)	
46-55	2131 (32.56)	1944 (32.90)	187 (29.40)		2078 (32.66)	53 (29.12)	
≥ 56	1410 (21.54)	1322 (22.37)	88 (13.84)		1370 (21.53)	40 (21.98)	
Mean ± SD	47.61 ± 8.74	47.82 ± 8.80	45.63 ± 7.94	<0.001	47.62 ± 8.74	47.34 ± 8.97	0.674
Gender-no (%)				<0.001			0.148
Male	2893 (44.20)	2497 (42.26)	396 (62.26)		2803 (44.05)	90 (49.45)	
Female	3562 (55.80)	3412 (57.74)	240 (37.74)		3660 (55.95)	92 (50.55)	

Education				0.003			0.615
Mean ± SD	9.53 ± 4.77	9.46 ± 4.78	10.18 ± 4.67		9.53 ± 4.78	9.35 ± 4.71	
Physical activity				0.23			0.007
Mean ± SD	39.90 ± 6.14	38.93 ± 6.09	38.62 ± 6.67		38.94 ± 6.14	37.70 ± 6.33	
BMI				<0.001			<0.001
Mean ± SD	28.09 ± 4.80	27.96 ± 4.84	29.34 ± 4.29		28.04 ± 4.79	30.16 ± 4.82	
Wealth score index				0.441			0.726
Mean ± SD	0.159 ± 0.95	0.156 ± 0.94	0.186 ± 1.03		.158 ± 0.95	0.183 ± 1.09	
Alcohol consumption-no (%)				<0.001			0.133
Yes	620 (9.48)	512 (8.67)	108 (17.01)		597 (9.39)	23 (12.71)	
No	5918 (90.52)	5391 (91.33)	527 (82.99)		5760 (90.61)	158 (87.29)	
Cigarette smoking-no (%)				0.323			0.88
Yes	1293 (19.78)	1158 (19.62)	135 (21.26)		1258 (19.79)	35 (19.34)	
No	5245 (80.22)	4745 (80.38)	500 (78.74)		5099 (80.21)	146 (80.66)	
Opium consumption-no (%)				0.212			0.199
Yes	1136 (1738)	1037 (17.57)	99 (19.59)		1111 (17.48)	25 (13.81)	
No	5402 (82.62)	4866 (82.43)	536 (84.41)		5246 (82.52)	156 (86.19)	
Tooth brushing (%)				<0.001			0.504
≤ 1/week	924 (14.29)	802 (14.03)	122 (19.77)		895 (14.53)	29 (16.48)	
2-6/week	2046 (32.30)	1837 (32.13)	209 (33.87)		1985 (32.23)	61 (34.66)	
≥ 1/day	3364 (53.11)	3078 (53.84)	286 (46.35)		3278 (53.23)	86 (48.86)	
Hypertension-no (%)				0.636			0.002
Yes	1271 (19.42)	1143 (19.34)	128 (20.13)		1219 (19.16)	52 (28.57)	
No	5274 (80.58)	4766 (80.66)	508 (79.87)		5184 (80.84)	130 (71.43)	
Diabetes-no (%)				0.012			0.01
Yes	1087 (16.61)	959 (16.23)	128 (20.13)		1044 (16.41)	43 (23.63)	
No	5458 (83.39)	4950 (83.77)	508 (79.87)		5319 (83.59	139 (76.37)	
Dyslipidemia-no (%)				<0.001			<0.001
Yes	4715 (72.11)	41.67 (70.58)	548 (86.3)		4558 (71.69)	157 (86.74)	
No	27.89 (26.54)	1737 (29.42)	87 (13.7)		1800 (28.31)	24 (13.26)	
CVD-no (%)				0.261			0.735

Yes	462 (7.06)	424 (7.18)	38 (5.97)		448 (7.04)	14 (7.69)	
No	6083 (92.94)	5485 (92.82)	598 (94.03)		5915 (92.96)	168 (92.31)	

Table 2 shows sociodemographic characteristics, personal habits and medical history of the study population by ALP and GGT. The frequency of ALP elevate was significantly higher in people who smoked cigarettes (P-value 0.015), consumed opium (P-value 0.004), and had a history of hypertension (P-value<0.001), diabetes (P-value<0.001), and dyslipidemia (P-value<0.001). Individuals with elevated ALP had significantly higher average age (P-value<0.001) and BMI (P-value 0.020), education level (P-value<0.001), physical activity (P-value 0.039), wealth score index (P-value<0.001), and the frequency of tooth brushing (P-value<0.001). The frequency of elevated GGT in people with a history of hypertension (P-value<0.001), diabetes (P-value<0.001), dyslipidemia (P-value<0.001) and CVD (P-value 0.024) was significantly higher. Individuals with elevated ALP had significantly higher average age (P-value 0.001) and BMI (P-value<0.001), education level (P-value 0.023), physical activity (P-value 0.007), wealth score index (P-value 0.026), and the frequency of tooth brushing (P-value 0.049) [12].

Table 2: Sociodemographic characteristics, personal habits and medical history of the study population by ALP and GGT (n=6544).

Characteristics	Overall (n=6544)	Elevated ALP		P-Value	Elevated GGT		P-Value
		No (n=6011)	Yes (n=534)		No (n=5942)	Yes (n=602)	
Age-year-no (%)				<0.001			0.001
35-45	3004 (45.90)	2829 (47.06)	175 (32.77)		2765 (46.53)	239 (39.70)	
46-55	2131 (32.56)	1931 (32.12)	200 (37.45)		1927 (32.43)	203 (33.72)	
≥ 56	1410 (21.54)	1251 (20.81)	159 (29.78)		1250 (21.04)	160 (26.58)	
Mean ± SD	47.61 ± 8.74	47.61 ± 8.72	49.87 ± 8.75	<0.001	47.49 ± 8.74	48.78 ± 8.72	<0.001
Gender-no (%)				0.647			0.195
Male	2893 (44.20)	2662 (44.29)	231 (43.26)		2641 (44.45)	251 (41.69)	
Female	3562 (55.80)	3349 (55.71)	303 (56.74)		3301 (55.55)	351 (58.31)	
Education				<0.001			0.023
Mean ± SD	9.53 ± 4.77	9.63 ± 4.74	8.42 ± 4.99		9.57 ± 4.76	9.1 ± 4.89	
Physical activity				0.039			0.007
Mean ± SD	38.90 ± 6.14	38.95 ± 6.16	38.38 ± 5.94		38.97 ± 6.19	38.26 ± 5.65	
BMI				0.02			<0.001
Mean ± SD	28.09 ± 4.75	28.05 ± 4.80	28.56 ± 4.75		27.94 ± 4.78	29.58 ± 4.75	
Wealth score index				<0.001			0.026
Mean ± SD	0.159 ± 0.95	0.176 ± 0.95	-0.038 ± 0.95		0.167 ± 0.95	0.076 ± 0.93	

Alcohol consumption-no (%)			0.257			0.884
Yes	620 (9.48)	562 (9.36)	58 (10.86)		564 (9.50)	56 (9.32)	
No	5918 (90.59)	5442 (90.64)	476 (89.14)		5372 (90.50)	545 (90.68)	
Cigarette smoking-no (%)			0.015			0.242
Yes	1293 (19.78)	1166 (19.42)	127 (23.78)		1185 (19.96)	108 (17.97)	
No	5245 (80.22)	4838 (80.58)	407 (76.22)		4751 (80.04)	493 (82.03)	
Opium consumption-no (%)			0.004			0.697
Yes	1136 (17.38)	1019 (16.97)	117 (21.91)		1035 (17.44)	101 (16.81)	
No	5402 (82.62)	4985 (83.03)	417 (78.09)		4901 (82.56)	500 (83.19)	
Tooth brushing (%)			<0.001			0.049
≤ 1/week	924 (14.59)	826 (14.19)	98 (19.07)		820 (14.25)	104 (17.99)	
2-6/week	2046 (32.30)	1861 (31.98)	185 (35.99)		1862 (32.35)	183 (31.66)	
≥ 1/day	3364 (53.11)	3133 (53.83)	231 (44.94)		3073 (53.40)	291 (50.35)	
Hypertension-no (%)			<0.001			<0.001
Yes	1271 (19.42)	1117 (18.58)	154 (28.84)		1119 (18.83)	151 (25.08)	
No	5274 (80.58)	4894 (81.42)	380 (71.16)		4823 (81.17)	451 (74.92)	
Diabetes-no (%)			<0.001			<0.001
Yes	1087 (16.61)	951 (15.82)	136 (25.47)		922 (15.52)	164 (27.24)	
No	5458 (83.39)	5060 (84.18)	398 (84.53)		5020 (84.48)	438 (72.76)	
Dyslipidemia-no (%)			<0.001			<0.001
Yes	4715 (72.11)	4281 (71.28)	434 (81.43)		4180 (70.41)	534 (88.85)	
No	1824 (27.89)	1725 (28.72)	99 (18.57)		1757 (29.59)	67 (11.15)	
CVD-no (%)			0.198			0.024
Yes	462 (7.06)	417 (6.94)	45 (8.43)		406 (6.83)	56 (9.3)	
No	6083 (92.94)	5594 (93.06)	489 (91.57)		5536 (93.17)	546 (90.7)	

Table 3 shows sociodemographic characteristics, personal habits and medical history of the study population by hematuria and proteinoria. The frequency of hematuria in women (P-value<0.001) and proteinuria in men (P-value<0.001) was significantly higher. The frequency of hematuria was higher in people with opium consumption (P-value 0.002) and significantly lower in people with a history of diabetes (P-value<0.001). People with hematuria had a significantly lower average BMI (P-value 0.015) and wealth score index (P-value<0.001), and a lower level of education (P-value 0.001).

The frequencyof proteinuria was significantly higher in people who smoked cigarettes (P-value 0.040), consumpted opium (P-value 0.023), and had a history of hypertension (P-value<0.001), diabetes (P-value<0.001), dyslipidemia (P-value<0.001), and CVD (P-Value<0.001). People with proteinuria had a significantly higher mean age (P-value<0.001) and BMI (P-value 0.001), education level (P-value<0.001), and wealth score index (P-value 0.002). And the frequency of tooth brushing was less (P-value 0.002) [13].

Table 3: Sociodemographic characteristics, personal habits and medical history of the study population byhematuria and proteinoria (n=6511).

Characteristic s	Overall (n=6511)	Hematuria		P-Value	Proteinoria		P-Value
		No (n=5341)	Yes (n=1170)		No (n=6264)	Yes (n=281)	
Age-year-no (%)				0.616			<0.001
35-45	3004 (45.90)	2454 (45.95)	532 (45.47)		1323 (21.12)	98 (34.88)	
46-55	2131 (32.56)	1744 (32.65)	378 (32.31)		2035 (3249)	96 (34.16)	
≥ 56	1410 (21.54)	1143 (21.40)	260 (22.22)		1323 (21.12)	87 (30.96)	
Mean ± SD	47.62 ± 8.75	47.59 ± 8.76	47.71 ± 8.71	0.687	47.48 ± 8.69	50.58 ± 9.36	<0.001
Gender-no (%)				<0.001			<0.001
Male	2886 (44.32)	2485 (46.53)	401 (34.27)		27.32 (43.61)	161 (57.3)	
Female	3625 (55.68)	2856 (53.47)	769 (65.73)		35.32 (56.39)	120 (42.7)	
Education				0.001			<0.001
Mean ± SD	9.537 ± 4.77	9.62 ± 4.79	9.12 ± 4.69		9.59 ± 4.76	8.22 ± 4.87	
Physical activity				0.943			0.736
Mean ± SD	38.91 ± 6.15	38.91 ± 6.28	38.9±5.5		38.91±6.16	38.78 ± 5.89	
BMI				0.015			0.001
Mean ± SD	28.09 ± 4.81	28.16 ± 4.77	27.78 ± 4.96		28.04 ± 4.77	29.21 ± 5.31	
Wealth score index				<0.001			0.002
Mean ± SD	0.159 ± 0.95	0.179.95 ± 1	0.072 ± 0.95		0.166 ± 0.95	0.013 ± 0.99	
Alcohol consumption-no (%)				0.119			0.365
Yes	619 (9.52)	522 (9.78)	97 (8.3)		589 (9.41)	31 (11.03)	
No	5885 (90.48)	4814 (90.22)	1071 (90.7)		5668 (90.59)	258 (88.97)	
Cigarette smoking-no (%)				0.153			0.04
Yes	1290 (19.83)	1076 (20.16)	214 (18.32)		1224 (19.56)	69 (24.56)	
No	5214 (80.17)	4260 (79.84)	954 (81.68)		5033 (80.44)	212 (75.44)	

Opium consumption-no (%)				0.002			0.023
Yes	1133 (17.42)	929 (17.41)	204 (17.47)		1073 (17.15)	63 (22.42)	
No	5371 (82.58)	4407 (82.59)	964 (82.53)		5184 (82.85)	218 (77.58)	
Tooth brushing (%)				0.787			0.002
≤ 1/week	919 (14.58)	753 (14.56)	166 (14.66)		865 (14.26)	59 (22.1)	
2-6/week	2036 (32.31)	1680 (32.50)	356 (31.45)		1966 (32.40)	80 (29.96)	
≥ 1/day	3347 (53.11)	2737 (52.94)	610 (53.89)		3236 (53.34)	128 (47.94)	
Hypertension-no (%)				0.322			<0.001
Yes	1264 (19.41)	1049 (19.64)	215 (18.38)		1159 (18.50)	112 (39.86)	
No	5247 (80.59)	4292 (80.36)	955 (81.62)		5105 (81.50)	169 (60.14)	
Diabetes-no (%)				<0.001			<0.001
Yes	1085 (16.66)	944 (17.67)	141 (12.05)		983 (15.69)	104 (37.01)	
No	5426 (83.34)	4397 (82.33)	1029 (87.95)		5281 (84.31)	177 (62.99)	
Dyslipidemia-no (%)				0.165			<0.001
Yes	4691 (72.11)	3868 (72.48)	823 (70.46)		4477 (71.53)	238 (85)	
No	1814 (27.89)	1469 (27.52)	345 (29.54)		1782 (28.47)	42 (15)	
CVD -no (%)				0.674			<0.001
Yes	460 (7.06)	374 (7.00)	86 (7.35)		421 (6.72)	41 (14.59)	
No	6051 (92.94)	4967 (93.00)	1084 (92.65)		58.43 (93.28)	240 (85.41)	

Table 4 shows the Sociodemographic characteristics, personal habits and medical history of the study population by GFR. The frequency of GFR decrease was lower in people who consumpted alcohol (P-value<0.001), opium (P-value<0.001) and smoked cigarettes (P-value<0.001), and it was significantly higher in women (P-value<0.001) and people with a history of hypertension (P-value<0.001), diabetes (P-value<0.001), dyslipidemia (P-value<0.001), and CVD (P-value<0.001). Individuals with decreased GFR had significantly higher mean age (P-value<0.001) and BMI (P-value<0.001), and lower levels of education (P-value<0.001) and physical activity (P-value<0.001)[14].

Table 4: Sociodemographic characteristics, personal habits and medical history of the study population by GFR (n=6545).

Characteristics	**Overall (n=6545)**	**Decreased GFR**		**P-Value**
		No(n=5708)	**Yes(n=837)**	
Age-year-no (%)				
35-45	3004 (45.90)	2802 (49.09)	202 (24.13)	<0.001
46-55	2131 (32.56)	1882 (32.97)	249 (29.75)	
≥ 56	1410 (21.54)	1024 (17.94)	386 (46.12)	
Mean ± SD	47.61 ± 8.75	46.77 ± 8.36	53.36 ± 9.15	<0.001

Gender-no (%)				
Male	2893 (44.20)	2641 (46.27)	252 (30.11)	<0.001
Female	3652 (55.80)	3067 (53.73)	585 (69.89)	
Education				
Mean ± SD	9.532 ± 4.77	9.68 ± 4.69	8.49 ± 5.19	<0.001
Physical activity				
Mean ± SD	38.90 ± 6.14	39.08 ± 6.33	37.71 ± 4.51 7.11	<0.001
BMI				
Mean ± SD	28.09 ± 4.80	27.92 ± 4.80	29.29 ± 4.67	<0.001
Wealth score index				
Mean ± SD	0.159 ± 0.95	0.164 ± 0.95	0.122 ± 0.98	0.235
Alcohol consumption-no (%)				
Yes	620 (9.48)	570 (10.00)	50 (5.98)	<0.001
No	5918 (90.52)	5132 (90.00)	786 (94.02)	
Cigarette smoking-no (%)				
Yes	1293 (19.78)	1190 (20.87)	103 (12.32)	<0.001
No	5245 (80.22)	4512 (79.13)	733 (87.68)	
Opium consumption-no (%)				
Yes	1136 (17.38)	1035 (18.15)	101 (12.08)	<0.001
No	5402 (82.62)	4667 (81.85)	735 (87.92)	
Tooth brushing (%)				
≤ 1/week	924 (14.59)	820 (14.84)	104 (12.87)	0.147
2-6/week	2046 (32.30)	17.95 (32.48)	251 (31.06)	
≥ 1/day	3364 (53.11)	2911 (52.68)	453 (56.06)	
Hypertension-no (%)				
Yes	1271 (19.42)	952 (16.68)	319 (38.11)	<0.001
No	5274 (80.58)	4756 (83.32)	518 (61.89)	
Diabetes-no (%)				
Yes	1087 (16.61)	885 (15.50)	202 (24.13)	<0.001
No	5458 (83.39)	4823 (84.5)	635 (75.87)	

Dyslipidemia-no (%)				
Yes	4715 (72.11)	4027 (70.59)	688 (82.49)	<0.001
No	1824 (27.89)	1678 (29.41)	146 (17.51)	
CVD no (%)				
Yes	462 (7.06)	361 (6.32)	101 (12.07)	<0.001
No	6083 (92.94)	5347 (93.68)	736 (87.93)	

Table 5 shows periodontal characteristics of the study population by ALT and AST. There was a significant difference between the elevated ALT and BOP. The frequency of ALT elevate was significantly higher in people who had BOP (P-value 0.042) [15].

Table 5: Periodontal characteristics of the study population by ALT and AST (n=6545).

Characteristics	Overall (n=6545)	Elevated ALT		P-Value	Elevated AST		P-Value
		No (n=5909)	Yes (n=636)		No (n=6363)	Yes (n=182)	
BOP				0.042			0.472
Yes	4811 (73.51)	4322 (73.14)	489 (76.89)		4673 (73.44)	138 (75.82)	
No	1734 (26.49)	1587 (26.86)	147 (23.11)		1690 (26.56)	44 (24.18)	
Calculus				0.224			0.637
Yes	5338 (81.56)	4808 (81.37)	530 (83.33)		5192 (81.60)	146 (80.22)	
No	1207 (18.44)	1101 (18.63)	106 (16.67)		1171 (18.40)	36 (19.78)	
CAL				0.901			0.142
Yes	3905 (59.66)	3527 (59.69)	378 (59.43)		3806 (59.81)	99 (54.4)	
No	2640 (40.34)	2382 (40.31)	258 (40.57)		2557 (40.19)	83 (45.6)	
Pocket				0.486			0.658
Yes	898 (13.72)	805 (13.62)	93 (14.62)		871 (13.69)	27 (14.84)	
No	5647 (86.28)	5104 (86.38)	543 (85.38)		5492 (86.31)	155 (85.16)	

Table 6 shows periodontal characteristics of the study population by ALP and GGT. There was a significant difference between the elevated ALP and CAL. The frequency of ALP elevate was significantly higher in people who had CAL (P-value 0.007) [16].

Table 6: Periodontal characteristics of the study population by ALP and GGT (n=6545).

Characteristics	Overall (n=6545)	Elevated ALP		P-Value	Elevated GGT		P-Value
		No (n=6011)	Yes (n=534)		No (n=5942)	Yes (n=602)	
BOP				0.282			0.09
Yes	4811 (73.51)	4429 (73.68)	382 (71.54)		4385 (73.80)	425 (70.6)	
No	1734 (26.49)	1582 (26.32)	152 (28.46)		1557 (26.20)	177 (29.4)	
Calculus				0.181			0.099
Yes	5338 (81.56)	4891 (81.37)	447 (83.71)		4861 (81.81)	476 (79.07)	
No	1207 (18.44)	1120 (18.63)	87 (16.29)		1081 (18.19)	126 (20.93)	
CAL				0.007			0.712
Yes	3905 (59.66)	3557 (59.17)	348 (65.17)		3550 (59.74)	355 (58.97)	
No	2640 (40.34)	2454 (40.83)	186 (34.83)		2392 (40.26)	247 (41.03)	
Pocket				0.534			0.418
Yes	898 (13.72)	820 (13.64)	78 (14.61)		821 (13.82)	76 (12.62)	
No	5647 (86.28)	5191 (86.36)	456 (85.39)		5121 (86.18)	526 (87.38)	

Table 7 shows periodontal characteristics of the study population by hematuria and proteinoria. There was a significant difference between the presence of hematuria and proteinuria with CAL. In people who had CAL, the frequency of hematuria was significantly lower (P-value 0.041) and the frequency of proteinuria was higher (P-value 0.023) [17].

Table 7: Periodontal characteristics of the study population by hematuria and proteinoria (n=6545).

Characteristics	Overall (n=6545)	Hematuria		P-Value	Proteinoria		P-Value
		No (n=5341)	Yes (n=1170)		No (n=6264)	Yes (n=281)	
BOP				0.455			0.634
Yes	4811 (73.51)	3937 (73.71)	850 (72.65)		4601 (73.45)	210 (74.73)	
No	1734 (26.49)	1404 (26.29)	320 (27.35)		1663 (26.55)	71 (25.27)	
Calculus				0.364			0.897
Yes	5338 (81.56)	4370 (81.82)	944 (80.68)		5108 (81.55)	230 (81.85)	
No	1207 (18.44)	971 (18.18)	226 (19.32)		1156 (18.45)	51 (18.15)	
CAL				0.041			0.023
Yes	3905 (59.66)	3222 (60.33)	668 (57.09)		3719 (59.37)	186 (66.19)	
No	2640 (40.34)	2119 (23.67)	502 (42.91)		2545 (40.63)	95 (33.81)	
Pocket				0.463			0.529

Yes	898 (13.72)	742 (13.89)	153 (13.08)		863 (13.78)	35 (12.46)	
No	5647 (86.28)	4599 (86.11)	1017 (86.92)		5401 (86.22)	246 (87.54)	

Table 8 shows periodontal characteristics of the study population by GFR. There was a significant difference between GFR decrease with pocket and CAL. The frequency of GFR decrease was significantly higher in people with CAL (P-value<0.001). But the frequency of GFR decrease was significantly lower in people who had pockets (P-value 0.043) [18].

Table 8: Periodontal characteristics of the study population by GFR (n=6545).

Characteristics	Overall (n=6545)	Decreased GFR		P-Value
		No (n=5708)	Yes (n=837)	
BOP				0.85
Yes	4811 (73.51)	4198 (73.55)	613 (73.24)	
No	1734 (26.49)	1510 (26.45)	224 (26.76)	
Calculus				0.875
Yes	5338 (81.56)	4657 (81.59)	681 (81.36)	
No	1207 (18.44)	1051 (18.41)	156 (18.64)	
CAL				<0.001
Yes	3905 (59.66)	3359 (58.85)	546 (65.23)	
No	2640(40.34)	2349 (41.15)	291 (34.77)	
Pocket				0.043
Yes	898 (13.72)	802 (14.05)	96 (11.47)	
No	5647 (86.28)	4906 (85.95)	741 (88.53)	

Table 9 shows the associations between the elevated liver enzymes (ALT, AST, ALP, GGT) and periodontal health indexes among study participants using the crude and adjusted models. In people with BOP, the chance of ALT elevate was 22% higher (p<0.05). But after removing the confounding factors, this effect was not seen (p>0.05). In people with CAL, the chance of elevating ALP was 29% higher, but this effect was not seen after removing the confounding factors. There was no significant relationship between other periodontal health indexes and elevated liver enzymes (ALT, AST, ALP, GGT) [19].

Table 9: The associations between the elevated liver enzymes (ALT, AST, ALP, GGT) and periodontal health indexes among study participants using the crude and adjusted models.

Variable	Elevated ALT		Elevated AST		Elevated ALP		Elevated GGT	
	Crude model	Adjusted model	Crude model	Adjusted model	Crude model	Adjusted model	Crude model	Adjusted model
BOP								
No	1	1	1	1	1	1	1	1

Yes	1.22 (1.01-1.48)	1.07 (0.87-1.32)	1.13 (0.80-1.60)	1.08 (0.75-1.55)	0.90 (0.74-1.09)	0.93 (0.76-1.15)	0.85 (0.71-1.02)	0.86 (0.71-1.04)
Calculus								
No	1	1	1	1	1	1	1	1
Yes	1.14 (0.92-1.42)	1.01 (0.80-1.28)	0.91 (0.63-1.32)	0.86 (0.57-1.27)	1.18 (0.93-1.49)	1.23 (0.95-1.60)	0.84 (0.68-1.03)	0.86 (0.68-1.07)
CAL								
No	1	1	1	1	1	1	1	1
Yes	0.99 (0.84-1.17)	1.01 (0.84-1.21)	O.80 (0.60-1.08)	0.81 (0.60-1.12)	1.29 (1.07-1.55)	1.18 (0.96-1.44)	0.97 (0.82-1.15)	0.92 (0.77-1.11)
Pocket								
No	1	1	1	1	1	1	1	1
Yes	1.08 (0.86-1.37)	1.04 (0.81-1.33)	1.10 (0.72-1.66)	1.09 (0.71-1.68)	1.08 (0.84-1.39)	1.00 (0.77-1.29)	0.90 (0.70-1.16)	0.89 (0.68-1.15)

Note: Adjusted model is adjusted for age (continuous variable), gender (male/female), education (continuous variable), wealth status index (continuous variable), smoking (yes/no), opium use (yes/no), alcohol consumption (yes/no), body mass index (continuous variable), activity level (continuous variable), hypertension (yes/no), diabetes (yes/no), dyslipidemia (yes/no), history of CVD (yes/no), and brushing frequency (categorical).

Table 10 shows the associations between the kidney health indexes (hematuria, proteinoria, GFR) and periodontal health indexes among study participants using the crude and adjusted models. In people with CAL, the chance of GFR decreasing was 31% higher ($p<0.05$). But after removing the confounding factors, this effect was not seen ($p>0.05$). There was no significant relationship between other periodontal health indexes and kidney health indexes (hematuria, proteinuria, GFR) [20].

Table 10: The associations between the kidney health indexes (hematuria, proteinoria, GFR) and periodontal health indexes among study participants using the crude and adjusted models.

Variable	Hematuria		Proteinuria		Decreased GFR	
	Crude model	Adjusted model	Crude model	Adjusted model	Crude model	Adjusted model
BOP						
No	1	1	1	1	1	1
Yes	0.95 (0.82-1.09)	0.96 (0.83-1.11)	1.07 (0.81-1.41)	1.21 (0.90-1.64)	0.98 (0.83-1.19)	1.12 (0.93-1.34)
Calculus						
No	1	1	1	1	1	1
Yes	0.93 (0.79-1.09)	0.97 (0.82-1.14)	1.02 (0.75-1.39)	1.11 (0.78-1.58)	.98 (0.82-1.19)	1.03 (0.83-1.26)
CAL						
No	1	1	1	1	1	1
Yes	0.87 (0.77-.99)	0.92 (0.80-1.05)	1.34 (1.04-1.72)	1.15 (0.87-1.51)	1.31 (1.13-1.53)	1.02 (0.86-1.21)

Pocket						
No	1	1	1	1	1	1
Yes	0.93 (0.77-1.12)	0.94 (0.77-1.14)	0.89 (0.62-1.28)	0.81 (0.56-1.18)	0.79 (0.63-0.99)	0.78 (0.62-1.00)

Note: Adjusted model is adjusted for age (continuous variable), gender (male/female), education (continuous variable), wealth status index (continuous variable), smoking (yes/no), opium use (yes/no), alcohol consumption (yes/no), body mass index (continuous variable), activity level (continuous variable), hypertension (yes/no), diabetes (yes/no), dyslipidemia (yes/no), history of CVD (yes/no), and brushing frequency (categorical).

Discussion

The objective of this study was to investigate the relationship between liver and kidney disease with periodontal disease.

We found that there was no significant relationship between periodontal health indexes and the elevate of liver enzymes (ALT, AST, ALP, GGT). Contrary to our study, in a study conducted by Widita, et al., in 2018, which aimed to investigate the relationship between clinical periodontal parameters and changes in liver enzymes levels over an 8-year period in the Japanese elderly population with an average age of 72 years, they concluded that the increase in ALT levels It is significantly related to CAL and probing depth, but no significant relationship was found between AST level and periodontal clinical indexes. This difference can be due to the difference in sample size and racial and age differences.

In line with the result of our study, in a study conducted by Kuroki, et al., in 2018 with the aim of investigating the relationship between the level of liver enzymes and alveolar bone loss, they concluded that there is a significant relationship between the measured level of liver enzymes and the highest amount of alveolar bone loss.

Contrary to our study, in a study conducted by Furuta, et al., in 2010 with the aim of investigating the relationship between periodontitis and liver disorders in 18 and 19-year-old Japanese students, they concluded that in men, having periodontitis was significantly associated with increased ALT levels, but there was no significant relationship between periodontitis and ALT in female students. This difference can be due to the difference in the average age of the studied community and the difference in race.

We found that there was no significant relationship between periodontal health indexes and kidney health indexes (hematuria, proteinuria, GFR). Contrary to the results of our study, in a study conducted by Han et al., in 2013 with the aim of investigating the relationship between chronic kidney disease and periodontitis in Korean adults, they concluded that there is a positive relationship between hematuria and decreased GFR with periodontitis, but there is a relationship between Proteinuria and periodontitis were not found. This difference can be due to the racial difference and the difference in the way periodontitis is diagnosed and defined.

In line with the results of our study, in a study done by Brotto, et al., in 2013 with the aim of investigating the relationship between periodontitis and kidney disorders by measuring kidney health indicators in two groups of people with periodontitis and the group without periodontitis, they concluded that severe periodontitis is not associated with changes in kidney function.

Contrary to the results of our study, in a study by Vanezuela, et al., In 2021, they concluded that periodontal disease may be associated with the development of chronic kidney disease. This difference can be due to the difference in the size of the study sample, racial differences, and differences in the measurement and type of periodontal and kidney health indicators.

Strengths of the study

The current study has several strengths, including the population-oriented nature of the study, the large statistical population and the control of confounding factors. Also, the information collected for this study was collected with high accuracy by trained dentists and users. However, there were also some limitations to the research. For example, due to the cross-sectional design, we cannot investigate the cause-effect relationship between liver and kidney disease and periodontal disease. Also, all the participants in our study were from the same Iranian population, so the results cannot be generalized to other races and populations.

Conclusion

Overall, this study suggests that there was no significant relationship between liver health indexes (ALT, AST, ALP, GGT) and kidney health indexes (hematuria, proteinuria, GFR) and periodontal health indexes. However, in order to prove these results, it is necessary to confirm the results of cohort studies of other populations and longitudinal and prospective studies.

Ethical Approval and Consent to Participate

This study was authorized by the ethics committee of Rafsanjan university of medical sciences (Ethical codes: ID: IR.RUMS.REC.1402.060). Written informed consent was obtained from the participants. The participants' data were kept confidential and were only accessible to the study investigators. All methods were performed in accordance with the relevant guidelines and regulations.

Data Availability

The persian adult cohort study Center at Rafsanjan university of medical sciences in Iran hosts the datasets used in the current investigation. The information is not publicly accessible. However, the corresponding authors can provide the data on reasonable request.

Consent for Publication

Not applicable.

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Competing Interests

There are no conflicts of interest, according to the authors.

Authors' Contributions

Raziyehsadat Rezvaninejad designed the study and supervised the project. Mohammad Hossein Rokn Rabei collected the data and prepared Tables. Parvin Khalili and Zahra Jamali performed the statistical analysis. Raziyehsadat Rezvaninejad and Mohammad Hossein Rokn Rabei wrote and revised the initial manuscript. All the authors read and approved the final manuscript.

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