

Oral health status of adult heart transplant recipients in China

A cross-sectional study

Ying Cao, MS, DDS^{a,b}, Xi Chen, DDS, PhD^{c,*}, Yixin Jia, MD, DDS^d, Yalin Lv, MS^b, Zheng Sun, MS, DDS^{e,*}

Abstract

Limited information on the oral health status of adult heart transplant recipients (HTRs) is known, and no available data exist in China. A prerequisite dental evaluation is usually recommended for patients' postorgan transplantation because lifelong immunosuppression may predispose them to infection spread.

The aim of this study was to investigate the oral health status of Chinese adult HTRs and determine the association between oral health status and history of heart transplantation (HT).

We carried out a cross-sectional study to collect clinical, demographic, socioeconomic, and behavioral data from 81 adult patients who received heart transplantation during 2014 to 2015 in China. Clinical examinations for the presence of dental plaque, dental calculus, dental caries, and periodontal health conditions were performed in a standardized manner by one trained examiner. Sociodemographic, socioeconomic, and behavioral data were self-reported using questionnaires. The prevalence of the above conditions was compared with 63 age- and sex-matched controls. General liner regression analysis was used to assess associations between mean number of decayed, missing, and filled teeth (DMFT) and mean community periodontal index of treatment needs (CPITN) scores and history of heart transplant.

Mean age of the HT group was 47.7 ± 12.2 years and men accounted for 69.1% of the sample. The overall median DMFT score in the HT group was 3 (1–5) and caries prevalence was 80.2%, which were similar to the control group ($P > .05$). The overall mean CPITN score of the HT group was 1.84, which was significantly higher than the control group (1.07, $P = .001$). Participants in the HT group had worse oral hygiene status and more teeth with probing depth ≥ 4 mm than controls ($P = .043$). Compared with participants who had no history of heart transplantation, HTRs presented worse periodontal health conditions (mean CPITN score, adjusted odds ratio (OR) = 1.39, 95% confidence interval (CI) = 1.12–1.71, $P = .003$) and similar dental caries status (DMFT score, adjusted OR = 0.58, 95% CI = 0.37–0.91, $P = .058$).

Periodontal health status was positively associated with history of heart transplantation in Chinese adult HTRs.

Abbreviations: BI = bleeding index, BMI = body mass index, CI-S = simplified calculus index, CPITN = community periodontal index of treatment needs, CsA = cyclosporine A, DI-S = simplified debris index, DMFT = decayed, missing, and filled teeth, GH = gingival hyperplasia, GLR = general liner regression, HT = heart transplantation, HTR = heart transplant recipient, OHI-S = simplified oral hygiene index, PD = probing depth, Tac = tacrolimus.

Keywords: dental caries, heart transplantation, oral health, periodontal disease

Editor: Cheng-Chia Yu.

The authors have no conflicts of interest to disclose.

^a Beijing Stomatological Hospital, ^b Department of Stomatology, Beijing Anzhen Hospital, Capital Medical University, Beijing City, China. ^c Department of Preventive and Community Dentistry, University of Iowa, Iowa City, ^d Department of Cardiac Surgery, Beijing Anzhen Hospital, ^e Department of Oral Mucosal Diseases, Beijing Stomatological Hospital, Capital Medical University, Beijing City, China.

* Correspondence: Zheng Sun, Beijing Stomatological Hospital, Capital Medical University, No. 4 Tiantan xili, Dong Cheng District, Beijing City 100050, China (e-mail: kayysunzheng@sina.com), Xi Chen, Department of Preventive and Community Dentistry, University of Iowa College of Dentistry, Iowa City, IA 52242 (e-mail: xxi_chen@hotmail.com).

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Medicine (2018) 97:38(e12508)

Received: 20 March 2018 / Accepted: 29 August 2018

<http://dx.doi.org/10.1097/MD.00000000000012508>

1. Introduction

Over the past 50 years, organ transplantation has become a widely accepted and successful method of treatment around the world that has enabled hundreds of thousands of patients to receive optimal therapeutic benefit.^[1] Owing to organ donation, a total of 231 organs were transplanted in China during 2013.^[2] Because all transplant recipients are under continuous immunosuppressive therapy to prevent chronic transplant rejection, they are more susceptible to the development of systemic complications and are at increased risk of oral and dental infections. Fungal infection, cytomegalovirus infection, gingival hyperplasia (GH), and malignant oral lesions may also arise as a direct result of immunosuppression or drug interactions.^[3,4]

Bacterial, viral, and fungal infections that arise among heart transplant patients are usually consequences of drug-induced immunosuppression.^[5] Routine dental care is important to reduce potential sources of infection during the drug-induced immunosuppression phase of heart transplantation. Several studies have drawn attention to inadequate oral hygiene behavior and increased dental and periodontal diseases among patients

receiving an organ transplant.^[6–9] Ziebolz et al^[10] revealed that the occurrence of dental caries is similar before and after solid organ transplantation, but organ transplant recipients experience more dental caries than the general population. Oral hygiene in patients with a solid organ transplant has been found to be significantly worse than that of patients on the transplant waiting list. Segura-Saint-Gerons et al^[11] found that Spanish heart transplant recipients had poor self-perceived oral health-related quality of life. However, data on the dental health status of heart transplant recipients (HTRs) are scarce in China. Given the increased number of transplants in recent years, the possibility is increased of a general dentist encountering a transplant patient who requires special dental care.^[1,2,12] Although some studies have been conducted among adults who undergo heart transplantation (HT) in other countries and regions, these studies have mostly focused on GH induced by immunosuppressive therapy and the effect of periodontal treatment on GH.^[13–16] However, the complete oral health profile remains unclear in this population. Therefore, it is of great importance to collect oral health information on HTRs.

Lifestyle and oral health-related behaviors (e.g., the frequency of tooth-brushing, frequency of eating snacks, dental utilization pattern) of HTRs may change after a transplant operation,^[17] which may contribute to dental neglect and increased risk of oral diseases. To obtain more information concerning dental and periodontal health status in these patients and better understand the impact of a history of heart transplantation on oral health, we conducted a cross-sectional study to describe the oral hygiene, dental, and periodontal status among adult HTRs in China, and to identify the potential differences in oral health between HTRs and controls. This information could be used to improve the oral health management of heart transplant patients.

2. Methods

2.1. Study design and study population

This cross-sectional study was conducted at Beijing Anzhen Hospital, affiliated to Capital Medical University, from January 2015 to December 2015. A total 81 HTRs who underwent heart transplantation surgery between January 2014 and September 2015 in the Department of Cardiac Surgery and 63 sex- and age-matched controls were recruited from the physical examination center of Anzhen Hospital. The control participants were neither receiving organ transplants nor under immunosuppressive therapy.

We excluded individuals meeting the following criteria: <18 years old, pregnant, with a history of periodontal treatment in the last 6 months, current serious systemic infection, addiction to alcohol or drugs, current seizure or any neurological disorders.

2.2. Ethics

Ethical approval was obtained from the Ethics Committee of Beijing Anzhen Hospital (Approval No. 2015017) prior to the implementation of the study, and written informed consent was obtained from all study participants.

2.3. Data collection

After providing their informed consent, all participants received a comprehensive oral examination and a survey using a structured questionnaire. Oral examinations were conducted at the Dental Department of Beijing Anzhen Hospital by a trained dentist in a standardized manner.

The Simplified Oral Hygiene Index (OHI-S), including the Simplified Debris Index (DI-S) and Simplified Calculus Index (CI-S), was used to assess the oral hygiene status of study participants. Dental caries were assessed using the World Health Organization 1997 criteria.^[18] The number of decayed (D), missing (M), and filled (F) teeth (DMFT) and caries prevalence were calculated to assess overall caries occurrence. Periodontal health was evaluated using probing depth (PD), bleeding index (BI), and the community periodontal index of treatment needs (CPITN). The CPITN score was recorded for 10 index teeth (17, 16, 11, 26, 27, 37, 36, 31, 46, and 47) using the following criteria: 0 = healthy; 1 = bleeding on probing; 2 = calculus; 3 = PD 4–5 mm; and 4 = PD 6 mm or more.^[16] The mean CPITN score was calculated for each participant. GH is characterized by an increase in gingival volume that is usually located in the gingival papillae. We documented all occurrence of GH among HTRs in this study.

In addition to oral examination, participants were asked to complete a structured questionnaire that included the following aspects: sociodemographic information, general health status and medication, oral health-related behaviors (e.g., snacking pattern, daily oral hygiene practice, and dental utilization in recent years), and self-perceived value of oral health. HTRs were also queried about the reason for heart transplantation, the date of transplant, as well as current immunosuppressive therapy.

The self-perceived value of oral health was measured using a questionnaire consisting of 13 items. For each question, participants were asked how they perceived the value of different aspects of oral health. Responses were recorded using a Likert-type scale (1 = no importance, 2 = little importance, 3 = does not matter, 4 = quite important, 5 = extremely important); 0 indicates no response. The sum of scores for the self-perceived value of oral health ranges from 0 to 65, with higher scores indicating a higher perceived value of oral health.

Prior to initiation of the study, the examiner was trained and calibrated to a gold standard examiner. Oral examinations were completed for 10% of the sample to assess examiner reliability. The minimal time interval between examinations was 2 days. Cohen's unweighted kappa for caries status at tooth level and periodontal conditions were 0.92 and 0.83, respectively.

2.4. Statistical analysis

Descriptive analyses were first conducted to compare socio-demographic, oral, and systemic characteristics between the HTRs and controls using the Student *t*-test (parametric data following a normal distribution), Mann-Whitney *U* test (nonparametric data), and chi-square test (categorical data). To assess the association between a history of HT and oral health, 2 multivariate regression analyses were conducted. First, a multivariate negative binomial regression was developed to study the association between a history of heart transplantation and dental caries, adjusting for sociodemographic and other confounders (i.e., sex, age, educational attainment, snacking frequency, tooth-brushing frequency, dental visit pattern, self-perceived value of oral health score, and body mass index (BMI)). A multivariate general liner model was developed to examine the association between a history of heart transplantation and periodontal health measured by CPITN score, adjusting for sociodemographic and other confounders (i.e., sex, age, educational attainment, smoking history, diabetes mellitus history, tooth-brushing frequency, dental visit pattern, self-

perceived value of oral health score, and BMI). The forward regression selection technique was used for model selection.

The .05 level was used as the criterion for statistical significance in all tests and model selections. All analyses were done with IBM SPSS version 22.0 (IBM Corp., Armonk, NY).

3. Results

The study sample consisted of 81 HTRs and 63 controls. Demographic, socioeconomic, and clinical characteristics of the study participants are detailed in Table 1. The mean age of the HT group was 47.7 ± 12.2 years and male participants accounted for 69.1% of the sample. The mean age of the control group was 49.6 ± 13.3 years and males accounted for 63.5% of the sample.

Age and sex distributions were similar in both groups, with no significant differences. Regarding educational level, nearly 80% of participants in the control group had a bachelor's degree, which was significantly more than the proportion in the HT group (30.9%, $P < .001$). The annual household income in the control group was also significantly higher than that in the HT group ($P < .001$).

Most HTRs received HT owing to cardiomyopathy. Among the 81 HTRs, 61 (75.3%) had cardiomyopathy, 11 (13.6%) had coronary atherosclerosis heart disease, 8 (9.9%) had valvular heart disease, and 1 (1.2%) had congenital heart disease, which were primary reasons for heart transplantation. In terms of immunosuppressive therapy, 35.8% of HT patients were taking cyclosporine A (CsA), mycophenolate-mofetil, and glucocorti-

Table 1
Characteristics of heart transplant recipients and control participants.

Variables	HT group N=81 (n,%)	Control group N=63 (n,%)	χ^2/t	P value
Gender				
Male	56 (69.1)	40 (63.5)	0.51	.476
Age, years, mean (SD)	47.7 (12.2)	49.6 (13.3)	-0.89	.373
<45	31 (38.3)	22 (34.9)	0.24	.888
45-55	33 (40.7)	26 (41.3)		
>55	17 (21.0)	15 (23.8)		
Educational attainment				
Junior or below	31 (38.3)	5 (7.9)	33.63	<.001
High school	25 (30.9)	8 (12.7)		
College or above	25 (30.9)	50 (79.4)		
Annual household income level				
Below CNY 100,000	64 (79.0)	29 (46.0)	29.24	<.001
Between CNY 100,000 to 200,000	8 (9.9)	21 (33.3)		
Above CNY 200,000	4 (4.9)	13 (20.6)		
Do not want to answer	5 (6.2)	0 (0.0)		
Comorbidity				
Hypertension	34 (42.0)	11 (17.5)	14.23	.002
Diabetes mellitus	25 (30.9)	9 (14.3)	7.46	.020
Hyperlipemia	11 (13.6)	4 (6.3)	0.20	.159
Combined with 2 kinds of systemic diseases or above	32 (39.5)	9 (14.3)	11.07	.01
Medicine				
Cyclosporine	53 (65.4)			
Tacrolimus	28 (36.6)			
Mycophenolatemofetil	79 (97.5)			
Glucocorticosteroid	43 (53.1)			
Calcium antagonists	9 (11.1)			
Heart disease				
Myocardopathy	61 (75.3)			
Coronal atherosclerosis heart disease	11 (13.6)			
Valvular heart disease	8 (9.9)			
Congenital heart disease	1 (1.2)			
Smoking				
Yes	14 (17.3)	19 (30.2)	3.32	.068
No	61 (82.7)	44 (69.8)		
Snacking frequency				
Fewer than once a day	10 (12.3)	15 (23.8)	3.25	.072
At least once a day	71 (87.7)	48 (76.2)		
Tooth-brushing frequency				
At least twice a day	41 (50.6)	38 (60.3)	1.35	.246
Fewer than twice a day	39 (56.8)	25 (39.7)		
Dental visit pattern				
At least once a year	8 (9.9)	14 (22.2)	4.17	.041
Irregularly	73 (90.1)	49 (78.8)		
Self-perceived value of oral health score, mean (SD)	55.73 (7.14)	55.65 (7.28)	0.71	.949
Body mass index (BMI), mean (SD)	24.40 (3.20)	23.18 (2.58)	0.45	.653

BMI=body mass index, HT=heart transplantation.

Table 2**Oral examination outcomes of the 2 participant groups.**

Variables	HT group N=81 (n,%)	Control group N=63 (n,%)	$\chi^2/Z/t$	P value
#Caries prevalence, n (%)	65 (80.2)	50 (79.4)	$\chi^2=0.17$.896
DMFT, Median (Q1,Q3)	3 (1,5)	3 (1,7)	Z=1.35	.052
DI-S, mean (SD)	0.90±0.52	0.61±0.39	t=3.70	.029
CI-S, M (Q1,Q3)	0.33 (0.17,0.83)	0.17 (0,0.17)	Z=1.73	.005
BI, mean (SD)	3.22 (0.84)	1.83 (0.66)	t=2.55	.042
teeth with PD≥4 mm, M (Q1,Q3)	5 (1,17)	4 (1,12)	Z=-1.05	.043
CPITN, mean (SD)	1.84 (0.74)	1.07 (0.54)	t=3.46	.001
GH, n (%)	24 (29.6)	0 (0)	$\chi^2=22.10$	<.001

BI=bleeding index, CPITN=community periodontal index of treatment needs, DMFT=decayed, missing, and filled teeth, DI-S=simplified debris index, GH=gingival hyperplasia.

#Caries prevalence refers to percentage of all participants with dental caries (DMFT ≥1; presence of one or more decayed or missing (M) teeth owing to caries, or filled teeth).

corticosteroids; 16.0% were taking tacrolimus (Tac), mycophenolate-mofetil, and glucocorticosteroids; 29.6% were receiving CsA and mycophenolate-mofetil; and 16.0% took Tac and glucocorticosteroids. Only 2.5% of HT patients were receiving monotherapy with only one immunosuppressive medication.

Hypertension was highly prevalent in all study participants but was more prominent among HTRs. About 42% of HTRs had hypertension, significantly higher than the proportion in the control group (17.5%, $P<.001$). Participants in the HT group was also more likely to have diabetes mellitus (30.9%) than those in the control group (14.3%, $P=.006$). HTRs had more chronic medical conditions than the controls. There was a greater proportion of patients with 2 or more systemic diseases in the HT group than in the control group (39.5% vs 14.3%, $P=.01$).

With respect to oral health-related behaviors, there were significantly more participants who regularly visited a dentist once or twice a year in the control group than in the HT group ($P=.041$). However, there was no statistically significant difference in smoking history, snacking frequency, tooth-brushing frequency, or self-perceived value of oral health score between the 2 groups.

Oral health outcomes are shown in Table 2. Dental caries prevalence did not differ between the groups (80.2% vs 79.4%, $P=.896$). The DMFT index was also similar in the 2 groups (median=3 in both, $P=.144$).

HTRs had worse oral hygiene status and more periodontal conditions than the control participants. On average, the DI-S (mean=0.90) and CI-S (mean=0.33) in the HT group were significantly higher than the DI-S (mean=0.61) and CI-S (mean=0.17) in the control group ($P=.029$, $P=.005$, respectively). BI, the number of teeth with PD ≥ 4 mm, and mean CPITN score in the HT group were statistically higher than those in the control group ($P=.042$, $P=.04300$, and $P=.001$, respectively). Of 53 HTRs who took CsA, 24 (40.7%) presented with GH, which was significantly higher than in HTRs who took Tac or other immunosuppressive drugs (0/28, $P<.001$).

A negative binomial model was chosen to study the relationship between dental caries and history of heart transplantation (Table 3). For occurrence of dental caries measured by the DMFT index, after adjusting for sex, age, educational level, tooth-brushing frequency, dental visit pattern, self-perceived value of oral health, and BMI, the history of heart transplantation was not significantly associated with DMFT ($P>.05$).

A general linear model was chosen to study the association between periodontal conditions and the history of heart transplantation (Table 4). For periodontal status measured by CPITN score, multivariable GLR analysis showed that a history

of heart transplantation was significantly associated with CPITN score (OR=1.38, 95% CI=1.121–1.710, $P=.003$), after adjusting for other factors include sex, age, educational attainment, snacking frequency, tooth-brushing frequency, dental visit pattern, self-perceived value of oral health score, and BMI.

4. Discussion

This study aimed to describe the oral health status among Chinese adult HTRs, and to investigate the associations between a history of heart transplantation and dental caries or periodontal diseases in these individuals. Our findings revealed that periodontal health was significantly associated with a history of heart transplantation whereas dental caries were not associated with heart transplantation history in the studied participants.

Heart transplantation is known to increase survival in patients with end-stage heart failure, but many patients still experience problems that affect their functional abilities after transplantation.^[19] In addition, they experience dramatic physiological and psychological changes and as well as a high treatment-related financial burden. High disease burden and intensive medical treatment may also induce oral complications.^[20–22] As these

Table 3**Relationships between DMFT scores of participants and selected independent factors, by negative binomial regression (n=144).**

Variables	OR	95%CI	P value
Group			
HT group	0.58	0.37–0.91	.058
Control group	1		
Educational attainment			
College or above	0.664	0.39–1.13	.130
High school	0.80	0.46–1.39	.421
Junior or below	1		
Tooth-brushing frequency			
At least twice a day	1.52	1.03–2.22	.053
Fewer than twice a day	1		
Dental visit pattern			
At least once a year	0.82	0.49–1.37	.444
Irregularly	1		
Self-perceived value of oral			
Health score	1.00	0.97–1.02	.815
Body mass index (BMI)	0.99	0.93–1.06	.718

Adjusted sociodemographic and other confounders include sex, age, educational attainment, snacking frequency, tooth-brushing frequency, dental visit pattern, self-perceived value of oral health score, and BMI.

BMI=body mass index, DMFT=decayed, missing, and filled teeth, HT=heart transplantation.

Table 4**Relationships between mean CPITN score of participants and selected independent factors, by general liner regression (n = 144).**

Variables	OR	95%CI	P value
Group			
HT group	1.39	1.12–1.71	.003
Control group	1		
Dental visit pattern			
At least once a year	0.73	0.56–0.94	.015
Irregularly	1		
Smoking			
Yes	1.47	1.15–21.87	.002
No	1		
Diabetes mellitus			
Yes	1.41	1.09–1.82	.009
No	1		
Self-perceived value of oral health score	0.98	0.97–1.00	.016

Adjusted sociodemographic and other confounders include sex, age, educational attainment, snacking frequency, tooth-brushing frequency, dental visit pattern, self-perceived value of oral health score, and body mass index.

CPITN=community periodontal index of treatment needs, HT=heart transplantation.

factors might affect activities of daily living in HTRs, some daily habits including oral hygiene and oral health behaviors may change after transplantation, which may increase the risk of dental and periodontal diseases. The present study showed that HTRs had higher DI-S and CI-S scores compared with control participants, indicating a worse oral hygiene condition among HTRs than in controls. Poor oral hygiene was the shared risk factor for dental caries and periodontal disease. Dental caries was one of the main oral infectious diseases observed among study participants. Dental caries prevalence varies among people according to age, sex, socioeconomic status, race, geographical location, food habits, and oral hygiene practices.^[23] As shown in this study, the HT group had poorer oral hygiene, lower annual household income, and were less likely to visit a dentist regularly, which may increase the risk of dental caries. However, the level of dental caries in the HTRs was similar to that in the controls. The present study also showed that the prevalence of dental caries in HTRs was lower than that in people aged 35 to 44 years and 65 to 74 years in China, according to the Third National Oral Health Survey in mainland China.^[24] A number of potential confounding factors such as educational level, tooth-brushing frequency, dental visit pattern, self-perceived value of oral health, and BMI were considered in the negative binomial regression model, but none of these were significantly associated with dental caries occurrence. This finding suggests that some other unmeasured factors may affect participants' dental caries experience. This requires further investigation in future studies.

HTRs have an increased risk of developing periodontal diseases as a result of long-term immunosuppressive therapy. The most commonly described condition in the literature is GH induced by CsA, with prevalence ranging from 5% to 70%, as reported in previous studies.^[25,26] The positive relationship between inflammation and GH is widely recognized.^[27,28] In the present study, two-thirds of HTRs routinely received CsA as immunosuppressive therapy, and nearly 40% (24 of 53) of HTRs who took CsA developed some degree of GH. GH greatly affects oral hygiene, chewing ability, and social activities, and increases the accumulation of dental plaque, which can cause periodontal disease. Thus, it is not surprising to observe that the BI score and number of teeth with PD \geq 4 mm in HTRs were significantly

higher than those in the control group, indicating worse periodontal status among HTRs.

Some risk factors such as poor oral hygiene, diabetes, smoking, medication, age, genetics, and stress are related to periodontal diseases. Recent longitudinal studies have suggested that long-term regular recipients of dental care have better oral health compared with non-regular recipients.^[29–31] In this study, the lack of access to regular dental care may escalate the risk of periodontal diseases in HTRs. Other factors might also contribute to the poor periodontal health of HTRs. Hyperglycemia, glucose intolerance, and diabetes mellitus are the most common metabolic disorders and clinically relevant complications after solid organ transplant. Diabetes can promote the occurrence, progression, and severity of periodontitis.^[32] In the present study, diabetes mellitus was highly prevalent in the HT group, with 30.9% of participants in the HT group diagnosed with diabetes mellitus, significantly higher than the proportion in the comparison group ($P < .001$). This can also be attributed to the worse periodontal conditions among HTRs.

CPITN has been widely used recently to measure the level of periodontal disease and define periodontitis.^[33] HTRs in our study had significantly higher CPITN scores than control participants, and the periodontal health condition of adult HTRs was positively associated with a history of heart transplantation after adjusting potential confounding factors such as sex, age, educational attainment, snacking frequency, tooth-brushing frequency, dental visit pattern, self-perceived value of oral health score, and BMI in the final general liner model.

Oral diseases and infection can compromise quality of life in individuals undergoing solid organ transplantation.^[34,35] Because a local oral infection may lead to systemic complications,^[33,36,37] patients requiring heart transplant should be carefully evaluated and treated for dental infections and good oral health status should be maintained during the pre- and postsurgical stages. This poses a challenge for dental professionals owing to the complex medical history of these patients. Because many HTRs are immunologically compromised, it is challenging to individualize dental treatment plans and determine the appropriate treatment and intensity to maintain health status among HTRs and thus, their ability to tolerate dental treatment. Management of these patients usually requires comprehensive oral and systemic assessment, careful planning, and good communication between dental providers, medical professionals, and patients.

As a cross-sectional study, this research has several limitations. First, the study includes a small sample size, which may limit its statistical power. Thus, future studies with larger sample sizes are needed, to support the present findings. Second, this cohort of patients was recruited in a single-center study at our hospital. Although ours is one of the largest cardiovascular disease hospitals in the country and admits patients from all parts of China, the data described herein cannot be extrapolated to the entire population of Chinese HTRs. Pooling of data from national databases on the oral health status of HTRs in multicenter studies will reinforce the generalizability of such findings. Finally, because the present study was a cross-sectional analysis, we did not collect precise information about the pre-transplant oral health status and oral health behavior of HTRs, which might affect the post-transplant oral health status and oral health behavior of HTRs in this study. Therefore, we were unable to assess how these factors may influence the oral health status of HTRs. Further clinical and basic research studies are required to clarify this issue.

5. Conclusions

The present study showed that periodontal health was poor among Chinese adult HTRs. Poor periodontal health was associated with a history of heart transplant in adult HTRs. However, the association between dental caries and heart transplantation history was uncertain. Collectively, these findings highlight the need for better management of the periodontal condition in patients who undergo heart transplantation. These patients should be carefully evaluated and treated for dental infections and good oral health should be maintained during the pre- and post-transplant stages.

Author contributions

Conceptualization: Ying Cao, Zheng Sun.

Data curation: Ying Cao.

Formal analysis: Ying Cao, Zheng Sun, Xi Chen.

Methodology: Ying Cao, Xi Chen, Yixin Jia, Zheng Sun.

Project administration: Ying Cao, Yalin Lv, Zheng Sun.

Software: Ying Cao, Xi Chen.

Supervision: Zheng Sun.

Validation: Ying Cao, Zheng Sun.

Writing – original draft: Ying Cao.

Writing – review & editing: Ying Cao, Xi Chen, Zheng Sun.

Ying Cao orcid: 0000-0003-0918-0581

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