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ORIGINAL ARTICLE

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Association between pulp stones and systemic diseases: A case-control study

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ABSTRACT

Introduction: Pulp stones (PS) are calcifications commonly found in the pulp tissue that may be associated with systemic diseases. **Objective:** To evaluate the association between PS and systemic diseases. **Methods:** A case-control study with the inclusion of individuals from 18 to 65 years of age, of both sexes. Analysis was made of 1047 digital panoramic radiographs. The controls could not have any teeth with PS; the cases were the contrary. A questionnaire comprising demographic, habit, and general health (diabetes, problems with blood vessels, altered cholesterol level, heart attack, kidney or gallbladder stone, arthritis, or autoimmune disease, and for women, endometriosis, and ovarian cyst). Data were submitted to the Student's t-test to identify differences between groups about sex and age. The Chi-square test was applied to the cross-tabulation. The analyses were performed using SPSS®, version 25.0, with a 5% significance level. **Results:** 490 patients participated (242 cases and 248 controls). There was no difference between groups for the sex (p=0.966) and age (p=0.186). Only “kidney stone” was associated with the case group (p=0.001), being almost three times higher when compared to the control group. No significant differences were found in females about the presence or absence of PS (p>0.05). **Conclusion:** In this research, it is suggested the existence of an association between kidney stones and the presence of pulp stones.

Keywords: dental pulp calcification; kidney calculi; radiography, panoramic; tooth diseases.

INTRODUCTION

Pulp stones (PS) are calcifications present in pulp tissue found in both healthy teeth and decayed or restored teeth. They are presented as radiographic findings the images of which are radiopaque inside the dental pulp[1]. Their shape and size are variable, and they can obstruct the pulp chamber, in some cases, endodontic intervention in teeth with PS becomes a challenge[1].

PS are asymptomatic and can be identified in young and elderly populations, but there is evidence that advancing age favors their appearance[2]. There are indications that the prevalence of PS is variable[3,4], with permanent molars being the most affected teeth[5].

The mechanisms involved in the formation of these calcifications have not yet been fully elucidated[6], which is why their etiopathogenesis has been widely discussed. It is suggested that traumatic occlusion[7], orthodontic movement[8,] and irritating factors, such as restorative materials that promote chronic inflammation[9], are the most frequent causal factors. However, genetic causes, nanoparticles, and nanobacteria can also be involved[10].

Histologically, the PS calcification pattern is amorphous, parallel to the blood vessels and nerves of the pulp, which classifies them as free, included, or fixed[1]. As the dental pulp is a living tissue that depends on continuous blood flow, any variant that interferes with its irrigation can affect it, generating PS[11].

Previous studies indicate that the presence of PS is associated with kidney stones[5,12] kidney disease diabetes[13] and cardiovascular diseases[5]. Thus, PS can serve as biomarkers for such conditions[14,15], being important to investigate this association, under the hypothesis that there is probably some aspect in common, related to the formation of calcifications.

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Based on the above, this case-control study aimed to test the hypothesis of an association between PS and systemic diseases in patients from a private Brazilian university.

METHODS

This study was approved by the Institutional Research Ethics Committee (approval no. 2.805.133). All participants signed the Free and Informed Consent Form. All procedures were by the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

The digital panoramic radiographs held in the image bank of the Radiology service of a private Brazilian university, taken between October 2018 and June 2019, were consulted. Using a total of 1047 images, a sample calculation was made for case-control studies. A 95% confidence level, 80% power, 5% error, effect size of 50%, and odds ratio (OR) of 1.7 were adopted, which resulted in n=229 for each group. A minimum of 5% was added to each group due to sample loss.

Patients of both sexes, aged between 18 and 65 years could be included. For allocation to the control group, the patient should have all teeth present and none of them could have an image suggestive of PS. For the cases, assessment of the posterior teeth (premolars and molars) was taken as standard, they could not be decayed and, if restored, the depth of the restoration had to be shallow (involvement of up to 1 mm of the amelodentinary junction).

Registration of the presence of PS occurred through the identification of a radiopaque mass defined inside the pulp chamber, regardless of size. As there was a

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need for confirmation using periapical radiography, of the "cases" pre-selected from the panoramic views, the researchers accessed their electronic medical records for additional images that could assist in decision-making; otherwise, patients were contacted by telephone and, if they met some criteria (desire to participate in the research, ability to understand what it was about, possibility of coming to the university, and women not being pregnant or suspected of being pregnant) they were invited to have radiographic exams at the university. The bisecting angle technique was adopted for the digital periapical radiography. When there was agreement between the previous radiographic findings (panoramic) and the periapical examination, patients were then allocated to the case group.

All patients answered a questionnaire containing demographic, habit, and general health variables. The questions were related to observed skin color (white, yellow, black, or brown) sex (male or female), age (in years), smoking (no or yes), frequent use of alcohol (no or yes), presence of diabetes (no or yes), type of diabetes (I or II), regular consultation with a cardiologist (no or yes), problems with veins/arteries (no or yes), altered cholesterol level (no or yes), heart attack (no or yes), kidney or gallbladder stone (no or yes) and arthritis or another autoimmune disease (no or yes). Women were also asked about having regular appointments with a gynecologist (no or yes), having endometriosis (no or yes), and having an ovarian cyst (no or yes).

This stage, of data collection, was conducted between July and November 2019. The image analysis was performed by two trained and calibrated researchers (kappa=0.88), on a computer screen under partial darkness of the room, at a standardized distance of 45 cm, to avoid bias in visualization due to greater or lesser proximity[11]. A third examiner, a specialist in radiology (gold standard) with 20 years of

https://doi.org/10.7322/abcshs.2022074.2137

experience, analyzed the selected images again to verify the diagnostic hypothesis raised. The questionnaire was also administered by previously trained researchers.

After the initial descriptive analysis, the data were submitted to Student's t-test to identify differences between groups (case and control), for the sex and age variables. Finally, cross-tabulations were performed using the Chi-square test. The results were expressed in OR and 95% confidence intervals (95% CI).

All analyses were performed using the SPSS® program (IBM® SPSS® Statistics v. 25.0, SPSS Inc, Chicago, USA), with a 5% significance level.

RESULTS

The final sample consisted of 490 individuals, 242 (49.4%) in the case group and 248 (50.6%) in the control group because Student's t-test did not reveal any difference between the case and control groups for the sex (p=0.966) and age (p=0.186) variables.

The mean age in the case group was 33.5 (SD=11.4) years, while in the control group, it was 32.1 (SD=10.8). Women represented 62.9% (n=308) of the sample, and those who declared themselves to be of white skin color accounted for 75.5% (n=370). Of the 21 individuals who claimed to have diabetes, three stated they were type I, eight stated they were type II and the rest were unable to inform their type. Of the women who participated (n=308), most confirmed consulting a gynecologist regularly (n=273; 88.6%), 39 (12.7%) reported having endometriosis and 63 (20.5%) ovarian cysts.

Table 1 shows the associations between the independent variables and the groups, with the respective 95% CI and p values. Only renal calculus was associated with the case group (p=0.001), so patients reporting the existence of this morbidity in this group were 2.77 times

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higher than in the control group. The other variables had no statistically significant differences ($p>0.05$).

Table 2 shows the data analyzed exclusively for females, in which no statistically significant difference was found in the analyses performed about any explanatory variable ($p>0.05$).

DISCUSSION

Since there is evidence of an association between systemic morbidities and PS, this research aimed to investigate this fact in individuals cared for at a private university in the city of Curitiba, Brazil. The results obtained allowed us to conclude that such an association did indeed occur, but only between PS and kidney stones.

Endodontic medicine has been gaining prominence in the scientific scenario after growing reports about the bidirectional relationship between periapical/endodontic conditions and systemic diseases[16]. Although it is not clear, it appears that the inflammatory process present in some systemic conditions is similar to that which occurs during the formation of PS. Amorphous aggregates of phosphorylated glycoproteins, including OPN, serve as initial sites for the precipitation of calcium crystals that give rise to PS, a mechanism similar to the formation of kidney stones, which result from the supersaturation of urine with calcium oxalate or calcium phosphate, proceeding to nucleation, growth, and aggregation of crystals[17]. It is observed that in both conditions these tissue changes follow the same pattern[18], which justifies the presence of calcifications in kidneys and pulp tissues in the same individuals. Studies suggest that an increase in the incidence of PS occurs with advancing age[2], as do the results of the present study. These findings can be supported

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by the fact that even non-erupted teeth can have PS[6], that is, they have not yet undergone any local stimulus that leads to the formation of PS.

Evidence indicates that PS is more common in women[2,14], but in the present study, there was no significant difference when comparing the participants' sex, agreeing with Udoye and Sede[19].

As for diabetes, Talla et al.[15] evaluated a total of 4,449 teeth from 2000 patients with diabetes, hypertension, and gastritis, whereby PS prevalence was significantly higher ($p<0.05$) among patients with morbidities. However, no association was found in the present research and only a small proportion of individuals self-reported diabetes. In turn, kidney stone was the variable in this research associated with PS, this being a fact also found previously. Movahhedian et al.[4], selected a total of 154 individuals, between cases and controls, to assess this relationship, and identified that the OR of an individual having a kidney stone was 5.78 times greater in those who had three or more teeth with PS which led the authors to state that the number of teeth with PS can be a predictor for the occurrence of kidney stones. The findings found here indicate that the presence of kidney stones was 2.4 times higher in the group of those with PS compared to controls. Gabardo et al.[12] in a systematic review, followed by meta-analysis, concluded that there is an association between PS and kidney stones, corroborating the results of this study.

In a study of 200 patients with chronic pulpitis, Aleksova et al.[20] evaluated pulps removed from patients with kidney and gallbladder stones and observed that they had small calcifications, confirming that there is an association between PS and kidney and gallbladder stones. However, in the present study, no data related to gallbladder stones were found. One of the reasons that can lead to these results stems from the method of

https://doi.org/10.7322/abcshs.2022074.2137

analysis since the accuracy of histological exams is superior in detecting small calcifications, as demonstrated by Aleksova et al.[20].

As for cardiovascular disorders, no association with PS was found in the present study, which differs from the findings of other authors[14,21]. In addition to observing that PS and carotid calcifications coexisted, Yilmaz et al.[21] identified changes in biochemical parameters in patients with a history of hemodialysis and diabetes, with increased levels of parathyroid hormone, calcium, and phosphorus.

Autoimmune diseases, with inflammatory characteristics, which have manifestations in the oral cavity, could be related to PS was evaluated here, but it was not confirmed, these being results that are in line with those of Nayak et al.[5].

This research sought to identify factors that could differ in some way between men and women, so associations between PS and endometriosis or ovarian cyst, for example, were investigated. The reason for this was based on the pathogenesis of diseases mediated by the immune system, with the formation and mineralization of dentin and bone, in addition to influencing pulp tissues and the periodontal ligament[22]. As for the methods adopted, it is worth making some considerations. It was observed that most studies on the association of PS and systemic diseases begin their investigation based on a group already diagnosed with systemic changes[4,5,20,21] and only then do PS begin to be observed. In the present study, the reverse was adopted. Thus, the observation of a PS during a radiographic examination can be useful once could be a biomarker, leading the dentist to warn the patient that he has a PS and that he should be aware of other possible systemic alterations.

The allocation of patients to the case and control groups was based on the analysis of images obtained using conventional radiographic examinations.

https://doi.org/10.7322/abcshs.2022074.2137

Despite the limitation attributed to this method, the literature supports this decision, with studies that use panoramic radiographs[8,11,21] and periapical radiographs[2,3,5,14]. It is known that histological exams and cone beam computed tomography are more reliable methods for early detection of PS[20] but requesting exams for patients with exposure to one more source of radiation or an invasive method was infeasible[22].

The limitation of this study is that complementary exams were not requested to prove the existence of systemic diseases, so the analyses were made based on patients' self-reports, who may be unaware of the existence of a disease, such as diabetes, for example. Also, the history of previous orthodontic treatment was not investigated, and this is a variable associated with the emergence of PS[8], which may represent a bias in the present study. Care was taken in the phase of allocating subjects to the case group, in the sense of not assessing teeth that had cavities or deep restorations, given the influence that these morbidities have on the development of PS[9].

The fact that in this study there was no significant difference between most of the variables evaluated may be related to the average age of the sample, 33.5 in the case group and 32.1 in the control group, since several chronic diseases can arise as age advances. However, about these averages, it should be noted that a positive aspect, in the sense of minimizing the impact of age on the development of PS, was the upper limit attributed to the age group (65 years), as also recommended by Kuzekanani et al.[3].

On the other hand, it was difficult to form a control group comprised of older individuals, since to be part of the control group all posterior teeth had to be present, and people are known to lose more teeth, especially the posterior ones, with advancing age. Consideration should also be given to the non-uniformity of the samples from the

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studies included in this discussion, as well as the analyses conducted in different and small ethnic groups. Finally, caution must also be taken regarding the interpretation of results considering objectives, limitations, analyses performed, and results, to generalize to the general population.

In sum, among the diseases studied here, it is suggested that there is an association between kidney stones and the presence of PS.

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Table 1: Association between the independent variables and case and control groups (n=490)

Variable	Group		OR (95%CI)	p*
	Case n (%)	Control n (%)		
Sex				
Male	90 (37.2)a	92 (37.1)a	1	0.928
Female	152 (62.8)a	156 (62.9)a	1.02 (0.69-1.50)	
Skin color				
White	185 (74.6)a	185 (76.4)a	1	
Yellow	16 (6.5)a	7 (2.9)a	0.80 (0.47-1.35)	0.188
Black	14 (5.6)a	10 (4.1)a	0.33 (0.12-0.93)	
Brown	33 (13.3)a	40 (16.5)a	0.61 (0.24-1.59)	
Smoking				
No	224 (92.6)a	223 (89.9)a	1	0.518
Yes	18 (7.4)a	25 (10.1)a	1.25 (0.64-2.43)	
Frequent use of alcohol				
No	214 (88.4)a	212 (85.5)a	1	0.302
Yes	28 (11.6)a	36 (14.5)a	1.34 (0.77-2.33)	
Diabetes				
No	231 (95.5)a	238 (96.0)a	1	0.545
Yes	11 (4.5)a	10 (4.0)a	0.75 (0.30-1.90)	
Regular consultation with a cardiologist				
Yes	107 (43.1)a	117 (48.3)a	1	0.117
No	125 (51.7)a	141 (56.9)a	1.36 (0.93-1.99)	
Problems with veins/arteries				
No	148 (61.2)a	152 (61.3)a	1	0.804
Yes	94 (38.8)a	96 (38.7)a	1.05 (0.71-1.54)	
Altered cholesterol level				
No	218 (90.1)a	219 (88.3)a	1	0.382
Yes	24 (9.9)a	29 (11.7)a	1.32 (0.71-2.48)	
Heart attack				
No	231 (95.5)a	232 (93.5)a	1	0.417
Yes	11 (4.5)a	16 (6.5)a	1.40 (0.62-3.12)	
Kidney stone				
No	201 (83.1)a	231 (93.1)b	1	**0.001**
Yes	41 (16.9)a	17 (6.9)b	0.34 (0.18-0.63)	
Gallbladder stone				
No	216 (89.3)a	221 (89.1)a	1	0.992
Yes	25 (10.3)a	26 (10.5)a	1.00 (0.54-1.84)	
Arthritis or other autoimmune disease				
No	235 (97.5)a	240 (96.8)a	1	0.354
Yes	6 (2.5)a	8 (3.2)a	1.71 (0.55-5.29)	

* Chi-square test. Different lowercase letters in the line indicate a statistically significant difference. Bold values are statistically significant ($p<0.05$).

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Table 2: Association between the independent variables and case and control groups with female data (n=308)

Variable	Group		OR (95% CI)	p*
	Case n (%)	Control n (%)		
Regular appointments with a gynecologist				
Yes	91 (84.3)a	139 (89.1)a	1	0.774
No	17 (15.7)a	17 (10.9)a	0.90 (0.44-1.83)	
Endometriosis				
No	93 (86.1)a	138 (88.5)a	1	0.470
Yes	15 (13.9)a	18 (11.5)a	0.78 (0.39-1.54)	
Ovarian cyst				
No	91 (84.3)a	119 (76.3)a	1	0.138
Yes	17 (15.7)a	37 (23.7)a	1.53 (0.87-2.69)	

* Chi-square test.

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