Original Research

Dental pulp stones and their correlation with metabolic diseases

Mohammad Imran Khan[1], Abhisheik Khare[1], Khushboo Arif[2], Sameera Shamim Khan[1], Abdullah Nasir[1], Shafik Lari[3]

[1]Department of Oral and Maxillofacial Pathology and Oral Microbiology, Career Post Graduate Institute of Dental Sciences and Hospital, Ghaila, IIM Road Lucknow, Uttar Pradesh, [2]Department of Public Health Dentistry, Faculty of Dental Sciences, King George's Medical University, Lucknow, Uttar Pradesh, [3]Department of Oral and Maxillofacial Pathology and Oral Microbiology, Chandra Dental College and Hospital, Safedabad, Lucknow, Uttar Pradesh, India

Abstract

Background: Dental pulp calcifications or pulp stones are calcified structures found in dental pulp, mostly around or enclosing a blood vessel. The formation of these calcifications begins with concentric layers of calcified tissue within which remnants of necrotic and calcified cells may be present. The calcifications of thrombi in blood vessels, called phleboliths, may also serve as nidi for denticles. In metabolic diseases such as diabetes, hypertension or poor periodontal health, there are obvious changes in blood vessels and vascularization. In our study, we observed histopathological sections of dental pulp and correlated systemic diseases such as diabetes and hypertension with poor periodontal health and dental pulp stones.

Aim: The aim of our study was to evaluate the histopathology of dental pulp stones, their distribution among various age groups and sexes and to identify any correlations between pulp stone formation and systemic diseases such as type II diabetes and hypertension.

Materials and Methods: Samples from 100 patients with metabolic diseases such as type II diabetes and hypertension were collected. The pulp was extirpated from the teeth that were undergoing root canal treatment, and the teeth were extracted. The collected pulp sample was fixed in 10% formaline neutral buffer, subjected to routine histopathological procedures and stained with haematoxylin and eosin. The pulp of teeth extracted for orthodontic treatment was considered a control for patients with no metabolic disease.

Results: There was a definite relationship between increased pulp stones and metabolic diseases such as type II diabetes and hypertension; likewise, poor periodontal health was significantly related to pulp stones.

Keywords: Denticles, diabetes, genetic origin, hypertension, pulp calcifications, pulp stones

Address for correspondence: Dr. Mohammad Imran Khan, 485/284 Jailor's Compound, Daliganj, Lucknow - 226 020, Uttar Pradesh, India.
E-mail: imranplz@yahoo.co.in

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INTRODUCTION

Pulp stones in the dental pulp and their association with systemic diseases are becoming an interesting area for research, providing a new platform for dental practitioners to correlate and predict the definite association of pulp stones with various systemic diseases, such as diabetes, renal stones, hyperlipidemia and cardiovascular diseases.

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Pulp stones can be used as biomarkers to assess systemic diseases or as a screening method for individuals who have multiple pulp stones found on routine intraoral radiographs, panoramic radiographs or cone beam computed tomography.[1]

Pulp stones are calcified or mineralized structures found in dental pulp distributed in coronal or radicular sections of the dental pulp.[2] Histopathologically, they are classified as true when they have a structure similar to that of dentin and have an odontoblastic layer peripherally, or falsely when there is mineralization around a nidus, most often a blood vessel.[3] They can be free-laid in fibrous pulp tissue or attached to the radicular dentinal wall.[4,5] The pathophysiology underlying pulp stone formation is not well understood, but multiple factors, such as advanced age, poor periodontal health, and various systemic conditions, mainly metabolic diseases such as diabetes and cardiovascular diseases such as atherosclerosis, have been shown to cause pulp stones.[6–8] Researchers have also reported correlations between pulp and renal stones.[9,10] With continuous, rigorous studies on nanobacteria or calcifying nanoparticles (CNPs), their association with pulp mineralization has also been considered.[11] Multiple pulp stones present on a radiograph within the pulp chambers may also suggest a genetic association with dentinal dysplasia.[12]

These pulp stones can cause various problems, such as idiopathic dental pain when pulp stones are associated with a nerve bundle, failure of root canal treatment due to obstruction, and perforation of the canal because of a misguided file pathway.[13,14] In addition to this, diabetic odontalgia is often encountered in type II diabetes patients, most likely because of impaired vascular collateral supply and poor immune response leading to ischemic pulp and necrosis, and this necrosis may serve as a nidus for mineralization in pulp tissue.[15] The effects of the advanced glycation end products (AGEs) of diabetes on elastin fibres, one of the major constituents of the extracellular matrix providing elasticity to blood vessels, are altered, leading to hypertension, as the pathogenesis of vascular diseases, including hypertension, is associated with elastin disorders.[16]

Another pathophysiology underlying the association of pulp stones with diabetes is the protein osteopontin (OPN), which has been found in peripherally strongly immunostained denticles.[5]

OPN is a multifunctional protein that is also related to hypertension and causes vascular remodelling, and its levels are increased in patients with type II diabetes.[17,18] Poor periodontal health in connection with type II diabetes is well documented because of reduced collagen turnover, vascular dysfunction, and thickening of gingival blood vessel walls, all of which can lead to tissue destruction.[19–21] In our study, we attempted to establish correlations between the frequency of pulp stones and systemic diseases such as type II diabetes, hypertension and oral periodontal health.

MATERIALS AND METHODS

A total of 100 patients were included in our study. Patients with type II diabetes, hypertension or poor periodontal health who underwent extraction or root canal treatment of their teeth were selected. The teeth that were extracted for orthodontic purposes were kept as controls with no systemic disease or periodontal issues.

Inclusion criteria: Patients who underwent root canal treatment, who underwent extractions, and patients whose teeth were extracted because of orthodontic treatment.

Exclusion criteria: Teeth with any periapical pathology, teeth with necrosed pulp, and deciduous dentitions.

METHODOLOGY

Patients who had been diagnosed with type II diabetes for more than five years and were receiving treatment for the disease were selected, along with patients who had hypertension, had been diagnosed with the disease for more than five years and were receiving antihypertensive treatment. All patients followed their routine treatment plan and follow-up. Patients were informed about the collection of the pulp sample from the tooth undergoing treatment, and informed consent was obtained from the patients. Patients with poor periodontal health were classified as stage 1 with no periodontal disease, stages 2 and 3 with moderate periodontal disease and stage 4 with poor periodontal health.

The pulp was extirpated from the teeth that were undergoing root canal treatment, and the teeth were extracted. The collected pulp sample was fixed in 10% formaline neutral buffer, subjected to routine histopathological procedures and stained with haematoxylin and eosin. The pulp of teeth extracted for orthodontic treatment was used as a control.

RESULTS

Statistical analysis

The results were analysed using descriptive statistics and comparisons among various groups. Categorical data are

summarised as proportions and percentages (%), and quantitative data are summarised as the mean ± standard deviation (SD).

The significance level was set at $P < 0.05$.

The demographic distribution of the study participants was analysed based on two variables: age and sex. Regarding age, the participants were divided into different groups. The largest age group was individuals between 40 and 49 years, accounting for 40.0% of the total sample. The second largest group consisted of individuals between 20 and 29 years, representing 16.0% of the sample. Participants below 20 years and between 50 and 59 years each constituted 7.0% of the total. Those aged 30–39 years and 60 years or older made up 15.0% each. The mean age of the participants was calculated to be 41.52 years, with a SD of 14.41 years.

In Table 1, terms of sex, the sample was predominantly male, with males accounting for 75.0% of the participants. Females, however, represented 25.0% of the total sample.

In Table 2, among the study participants (n = 100), comorbidities were analysed, and two specific conditions were focused on: diabetes and hypertension. The prevalence of diabetes among the participants was 26.0%, with 26 individuals out of the total sample being diagnosed with this condition. Hypertension, another commonly observed comorbidity, was found in 22 participants, accounting for 22.0% of the total sample.

Table 3 presents the distribution of periodontal health conditions among a sample of individuals. The data indicate that among the 100 individuals assessed, 26 individuals (26.0%) were classified as being in stage 1 of periodontal health. Additionally, 22 individuals (22.0%) were in stages 2 and 3, while the majority of the sample, comprising 52 individuals (52.0%), was identified as being in stage 4.

Table 4 reveals the presence and distribution of pulp stones among a sample of individuals. Out of the 100 individuals assessed, 35 individuals (35.0%) were found to have no pulp stones. Conversely, the majority of the sample, consisting of 65 individuals (65.0%), exhibited the presence of pulp stones.

Table 5 explores the relationship between comorbidities (specifically diabetes and hypertension) and the presence of pulp stones. The data included the number and percentage of individuals with and without each comorbidity, along with the corresponding Chi-square values, *P* values, odds ratios (ORs), and 95% confidence intervals (CIs) for the ORs.

Table 1: Distribution of subjects according to age and sex

Variable		No.	%
Age	<20 yr	7	7.0
	20–29 yr	16	16.0
	30–39 yr	15	15.0
	40–49 yr	40	40.0
	50–59 yr	7	7.0
	≥60 yr	15	15.0
	Mean±SD	41.52±14.41 yr	
Sex	Male	75	75.0
	Female	25	25.0

Table 2: Distribution of subjects according to comorbidities

Comorbidities	No. (*n*=100)	%
Diabetes	26	26.0
No metabolic disease	52	52.0
Hypertension	22	22.0

Table 3: Distribution of subjects according to periodontal health condition

Periodontal health condition	No.	%
Stage 1	26	26.0
Stages 2 and 3	22	22.0
Stage 4	52	52.0
Total	100	100.0

Table 4: Distribution of subjects according to pulp stone status

Pulp stone	No.	%
No	35	35.0
Yes	65	65.0
Total	100	100.0

For diabetes, among the individuals without diabetes, 32 individuals (43.2%) had no pulp stones, while 42 individuals (56.8%) had pulp stones. This serves as the reference category for comparison. In contrast, among individuals with diabetes, only three individuals (11.5%) had no pulp stones, while 23 individuals (88.5%) had pulp stones. The Chi-square value for the association between diabetes and pulp stones was 8.501, with a *P* value of 0.004. The ORs for individuals with diabetes compared to those without diabetes was 8.501, indicating a statistically significant association. The 95% CIs for the ORs ranged from 1.61 to 21.18, suggesting a greater likelihood of having pulp stones among individuals with diabetes.

Similarly, among individuals without hypertension, 33 individuals (42.3%) had no pulp stones, while 45 individuals (57.7%) had pulp stones. This serves as the reference category. In comparison, among individuals with hypertension, only two individuals (9.1%) had no pulp

Table 5: Association of comorbidities with pulp stones

Comorbidity		Pulp stone		Chi sq	*P*	OR	95 CI for OR
		Absent *n* %	Present *n* %				
Diabetes	No	32 (43.2%)	42 (56.8%)	Ref.	-	-	-
	Yes	3 (11.5%)	23 (88.5%)	8.501	0.004	5.84	(1.61–21.18)
Hypertension	No	33 (42.3%)	45 (57.7%)	Ref.	-	-	-
	Yes	2 (9.1%)	20 (90.9%)	8.322	0.004	7.33	(1.60–33.58)

stones, while 20 individuals (90.9%) had pulp stones. The Chi-square value for the association between hypertension and pulp stones was 8.322, with a *P* value of 0.004. The OR for individuals with hypertension compared to those without hypertension was 8.322, indicating a significant association. The 95% CIs for the ORs ranged from 1.60 to 33.58, indicating a greater probability of having pulp stones among individuals with hypertension.

These findings demonstrate a statistically significant relationship between diabetes and hypertension with the presence of pulp stones. Individuals with these comorbidities appear to be at a greater risk of having pulp stones than those without these conditions. These results underscore the importance of considering and addressing the potential impact of comorbidities on dental health, particularly in relation to pulp stone formation.

Table 6 gives an analysis of the age distribution among individuals with and without diabetes and hypertension status, and several patterns that emerge. Across different age groups, individuals aged less than 20 years and those between 20 and 29 years showed a 100% prevalence of no diabetes and no hypertension, with no cases of diabetes or hypertension reported. In the 30–39-year-old age bracket, while the majority (93.3%) did not have diabetes, a small percentage (6.7%) had diabetes, and all individuals were free from hypertension. Notably, in the 40–49-year-old age group, a higher proportion (70.0%) had no diabetes, while a significant minority (30.0%) had diabetes, and the distribution of hypertension status mirrored this pattern. For individuals aged between 50 and 59 years, a larger proportion (57.1%) had diabetes compared to those without, and a similar trend was observed for hypertension status. Among individuals aged 60 years and above, the prevalence of diabetes increased to 60.0%, with a corresponding decrease in those without diabetes, and a similar distribution was observed for hypertension status. The significance tests revealed a Chi-square value of 23.9 with a *P* value less than 0.001 for diabetes status and a Chi-square value of 20.1 with a *P* value of 0.001 for hypertension status, indicating statistically significant associations between age, diabetes, and hypertension.

Table 6: Association of age with diabetes and hypertension

Age	Diabetes status		Hypertension status	
	No diabetes *n* %	Diabetes *n* %	No hypertension *n* %	Hypertension *n* %
<20 yr	7 (100.0%)	0 (0.0%)	7 (100.0%)	0 (0.0%)
20–29 yr	16 (100.0%)	0 (0.0%)	16 (100.0%)	0 (0.0%)
30–39 yr	14 (93.3%)	1 (6.7%)	15 (100.0%)	0 (0.0%)
40–49 yr	28 (70.0%)	12 (30.0%)	28 (70.0%)	12 (30.0%)
50–59 yr	3 (42.9%)	4 (57.1%)	3 (42.9%)	4 (57.1%)
≥60 yr	6 (40.0%)	9 (60.0%)	9 (60.0%)	6 (40.0%)
Significance	Chi-square=23.9, *P*<0.001		Chi-square=20.1, *P*=0.001	

Table 7 examines the relationship between comorbidities (specifically periodontal health status) and the presence of pulp stones. The data included the number and percentage of individuals with and without each stage of periodontal health, along with the corresponding Chi-square values, *P* values, ORs, and 95% CIs for the ORs.

Among individuals with stage 1 periodontal disease, 20 individuals (76.9%) had no pulp stones, while six individuals (23.1%) had pulp stones. This serves as the reference category for comparison. Regarding stages 2 and 3 of periodontal health, three individuals (13.6%) had no pulp stones, while 19 individuals (86.4%) had pulp stones. The Chi-square value for the association between stages 2 and 3 and pulp stones was 19.13, with a *P* value less than 0.001. The OR for individuals in stages 2 and 3 compared to stage 1 was 19.13, indicating a strong and statistically significant association. The 95% CIs for the ORs ranged from 4.61 to 96.67, suggesting a significantly greater likelihood of having pulp stones among individuals with stage 3 periodontal disease.

Similarly, for stage 4 periodontal health, 12 individuals (23.1%) had no pulp stones, while 40 individuals (76.9%) had pulp stones. The Chi-square value for the association between stage 4 disease and pulp stones was 20.77, with a *P* value less than 0.001. The OR for individuals in stage 4 compared to stage 1 was 20.77, indicating a strong and statistically significant association. The 95% CI for the OR ranged from 3.64 to 33.97, suggesting a significantly greater probability of pulp stones among individuals with stage 4 periodontal disease.

Table 7: Association of periodontal health status with pulp stones

Comorbidity		Pulp stone		chi sq	*P*	OR	95 CI for OR
		Absent *n* %	Present *n* %				
Periodontal health status	Stage 1	20 (76.9%)	6 (23.1%)	Ref.	-	-	-
	Stages 2 and 3	3 (13.6%)	19 (86.4%)	19.13	<0.001	21.11	(4.61–96.67)
	Stage 4	12 (23.1%)	40 (76.9%)	20.77	<0.001	11.11	(3.64–33.97)

These findings demonstrate a substantial and statistically significant relationship between periodontal health status and the presence of pulp stones. Individuals in stages 2 and 3 and stage 4 of periodontal health appear to be at a significantly greater risk of having pulp stones than those in stage 1. These results emphasise the importance of considering the impact of periodontal health on dental conditions such as pulp stone formation, highlighting the need for effective management and intervention in individuals with advanced stages of periodontal disease.

DISCUSSION

Pulp stones are calcified entities found in dental pulp most commonly in older individuals, but with the increased interest of researchers in their pathophysiology, many studies have found serious associations between these conditions and systemic diseases.[3,22] The multifactorial effects of metabolic diseases, such as diabetes, are strongly related to the development of pulp stones in long-standing individuals with this disease.[23] We studied histopathological pulp sections from patients with diabetes and reported increased fibrosis of connective tissue in the skin, similar to the findings of a previous study by Argyropoulos *et al*.[24] The increased glycation of collagen can play a key role in diabetes-related fibrosis.[25] The accumulation of AGEs disturbs collagen molecule crosslinking, which is attributed to increased vascular damage in this disease.[26] The altered expression of collagenases leads to the accumulation of collagen and disturbances in other extracellular matrix proteins, such as laminin and fibronectin.[13] Experimentally induced hyperglycemia in rats also showed arteriosclerotic changes and an increased density of fibrous connective tissue.[27]

These pulp stones can cause obstruction in the radicular canal, causing failure of root canal treatments, breakage of instruments in the canal or perforation because of an incorrect guide path for the dental files.[28,29] Hyperglycemia also causes reduced bond strength, especially of composite resins, to hard structures of teeth, such as enamel and dentin.[30] It has been observed that there is greater accumulation and expression of type I and type IV collagen in hyperglycemic patients.[31] Polarisation microscopy using Picrosirius stain revealed that collagen type I was the main constituent of the dental pulp connective tissue matrix. Collagen types I, III, IV, V and VI are present in human dental pulp throughout life, and types I, III and VI are the main collagens involved in the composition of dental pulp stones.[13]

It is well established that hyperglycemia causes microvasculature disturbances, such as thickening of vessel walls and reduced vessel elasticity. All of these changes were observed in our study in histopathological sections of the dental pulp of patients with type II diabetes. Vascular changes in blood vessels are also responsible for the development of hypertension as a consequence of arteriosclerosis pathogenesis, which involves changes in elastin, an extracellular matrix protein, and the accumulation of collagen, leading to the thickening of vessel walls.[32,33]

An immunohistochemical study of dental pulp stones performed by Goga *et al*.[5] revealed collagen type I distribution throughout the mineralized tissue and strong immunostaining for OPN. OPN is a multifunctional protein that is expressed at relatively high levels in both type II diabetes and hypertension patients, and it plays a potential role in a variety of cardiovascular diseases, including atherosclerosis and vascular calcifications.[34–39] The calcifications or mineralized structures found in dental pulp are also often found in association with blood vessels. In a study on rat dental pulp tissue by Yuji Inagaki *et al*.,[40] OPN was associated with pulp calcifications in diabetic pulp tissue and plays an integral part in the mineralization front of calcification entities. Edds *et al*. studied the relationship between pulp stones and CVD and reported that calcification in larger vessels is similar to calcification in smaller vessels, supporting our findings of increased and definite dental pulpal calcifications in patients with vascular hypertension.[1,41,42]

Jinfeng Zeng *et al*. reported that CNPs are one of the etiological factors for the development of pulp stones. They explained that nanoparticles could produce biogenic carbonate apatite on their cell envelope, resulting in mineralization, which was comparable to other calcifications of tissue in humans, and hypothesised that CNPs can be an etiological factor behind dental pulp stones.[11,43]

To date, various studies have been performed to assess dental pulp calcifications associated with CVD on the basis of dental radiographs, but very few studies have used histopathological examination of pulp to confirm and determine the actual frequency of pulp calcifications. Histopathological examination reveals the actual frequency and types of pulpal calcifications, the status of pulp connective tissue, and the degree and type of inflammation, which all provide a better understanding of and correlation with systemic diseases.

In our study, we found a statistically significant relationship between pulp stones and hypertension, type II diabetes and poor periodontal health. The presence of pulpal stones on dental radiographs can be used as a screening method for patients to undergo further systemic evaluation for any associated disease, especially diabetes and hypertension. Histopathological examination confirmed the findings of earlier studies performed with dental radiographs of pulp stones associated with systemic disease, which are more frequent than what appears on radiographs, and if the size of pulpal calcification is small, it can be missed in routine radiological examinations, which is clearly evident in histopathological sections [Figure 1a and b]. Additionally, histopathological evaluation revealed the surface morphology and calcification pattern of the pulp stones [Figure 1c and d]. Multiple small rough surface stones to smooth surfaces with lamellar patterns of calcification or mineralization were observed under a microscope [Figure 1e]. There were multiple rough surface stones, while the smooth surface stones were larger in size and were found in singular forms [Figure 1f and g].

The pulp of subjects with diabetes appeared to be infiltrated with acute or chronic inflammatory infiltrates and thickened blood vessel walls [Figure 1h]. In some tissue sections, foci of degeneration were also observed. In poor periodontal conditions with mobile teeth, the pulp was

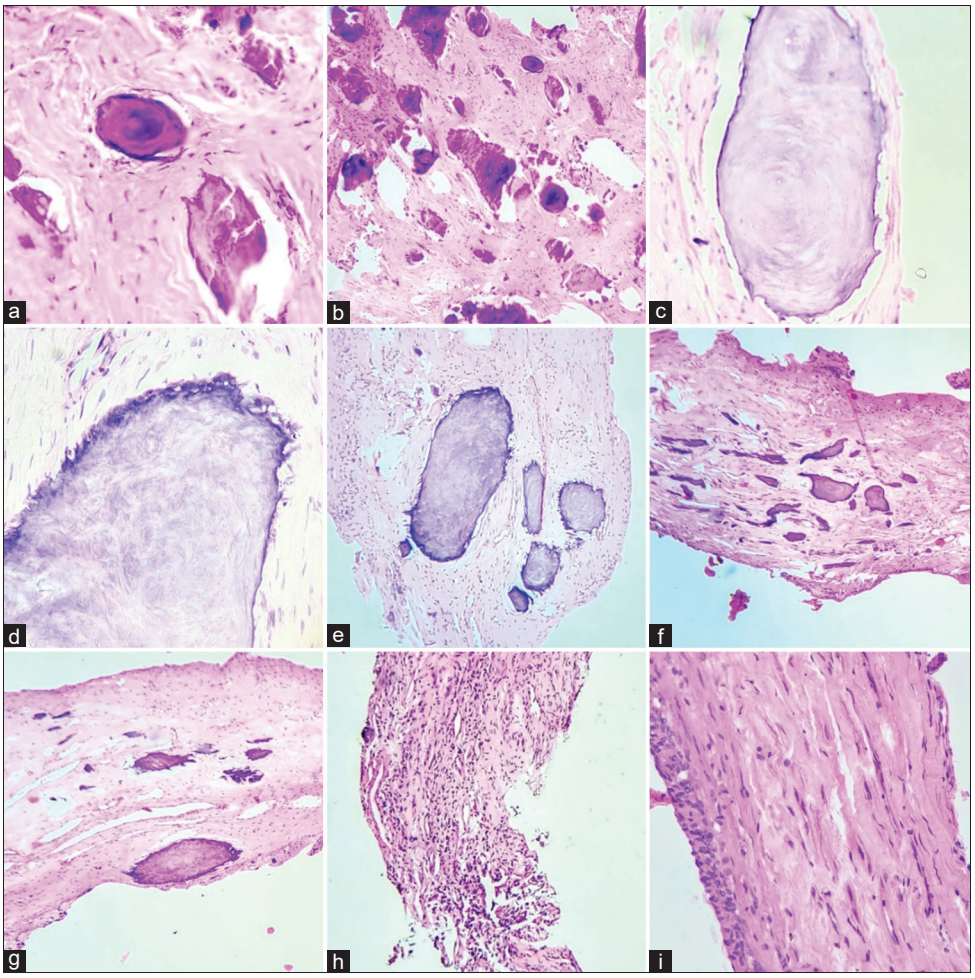

Figure 1: (a and b) Different types of pulp stones. (c) Sections showing the lamellate pattern of pulp stones. (d) Rough surface pulp stone. (e) Multiple pulp stones in the apex region. (f) Multiple small irregularly shaped pulp stones. (g) Attachment of pulp stone to the radicular wall. (h) Diabetic pulp tissue with intense inflammation. (i) Aged pulp with fibrous connective tissue and few foamy histiocytes in the thinned odontoblastic zone

mostly degenerated, and those teeth were excluded from the study. The sections obtained from poor periodontal health patients showed a marked inflammatory response with a thinned odontoblastic zone, and the inflammatory infiltrate was a chronic inflammatory infiltrate. Sometimes foamy histiocytes were also observed just below the zone of the odontoblastic layer. The pulp of older individuals showed marked atrophy of pulp with few fibroblasts in the focus and few blood vessels, indicating fibrous and atrophic changes in the pulp [Figure 1i]. Our observations were similar to those made by Puscasu *et al*.[44] for the histological appearance of the diabetic dental pulp.

CONCLUSION

Pathological calcifications or pulp stones in dental pulp are common in aged pulp, but recently, various systemic diseases, such as pulp stones with carotid artery calcifications, as observed on panoramic radiographs, renal calculi, cardiovascular diseases and metabolic diseases, have been associated with these conditions. We studied histopathological sections and found that pulp stones were significantly correlated with type II diabetes and hypertension. The histopathological examination provided more accurate knowledge about calcifications, even those of much smaller sizes, which can be missed in routine radiography. Along with knowledge of pulp calcifications that are being found on panoramic radiographs, bitewings or any other advanced radiological techniques and confirmation of their association with systemic conditions can provide a baseline tool to use pulp stones as a biomarker for screening subjects for further evaluation of any associated systemic disease. Our study provides a platform to further investigate what we found and confirmed via histopathological evaluation of dental pulp.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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