Pulp Stones: Diagnostic Significance in Early Diagnosis and Radiographic Correlation with Ischemic Heart Diseases

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Context and Aim  Sufficient evidence exists in the literature which indicates that patients with ischemic heart diseases (IHDs) show higher degree of pulp calcifications. The present study was, therefore, planned to estimate the prevalence of pulp stones in patients diagnosed with/or undergoing treatment for IHDs.

Materials and Methods  The present study, which consisted of 300 subjects within the age range of 25 to 65 years, was divided into two groups: study group comprising 150 patients (113 males and 37 females) and 150 age- and sex-matched healthy controls. Pulp stones were imaged using bitewing radiographs and paralleling technique under standard conditions.

Statistical Analysis Used  Statistical analysis was done using IBM SPSS Statistics for Windows version 21 (IBM Corp, Armonk, USA), while independent t-test and Chi-square test were done to check the prevalence of pulp stones in the study and control groups, based on gender-, arch-, region- and side-wise distribution. $p < 0.05$ was considered statistically significant.

Results  The patients with IHDs exhibited 100% prevalence of pulp stones and the difference was found to be statistically significant, although there was a significant difference in the mean number of pulp stones observed in the study and control groups, with the study group revealing 2217 pulp stones as against 639 pulp stones observed in the control group ($p < 0.001$). Furthermore, maxillary arch and posterior teeth were predominantly affected in both the groups, although the difference was not found to be statistically significant.

Conclusions  The findings of the present study suggested a positive correlation between pulp stones and IHDs, highlighting the significance of dental radiographic examination, which may have a possibility for an early detection of IHDs.
Introduction

Pulp stones are discrete calcifications appearing within the pulp of the healthy, diseased and/or, even, the unerupted teeth. They may exist freely within the pulp tissue or, may be attached to, embedded in dentin.\textsuperscript{1} Despite several microscopic and histochemical studies, the exact cause of pulp calcifications remains largely unknown; however, several conditions have been claimed to predispose to pulp stone formation, such as age, genetic predisposition, low-grade, persistent insults to the vital tissue, circulatory disturbances, and inductive interaction between the pulp tissue and the epithelium, although, in many instances, there is no clear-cut or defined etiology behind such degenerative changes, eventually leading to pulp calcifications. The latter category of changes where the etiology is not discernible is included as idiopathic calcifications.\textsuperscript{2-5}

Numerous studies have also shown an association between the formation of pulp stones and atheromatous plaques in the vessels.\textsuperscript{6-8} Likewise, Edds et al suggested that 74\% of patients with reported cardiovascular disease had detectable pulp stone formations, while only 39\% of patients without a history of cardiovascular disease had pulp stones.\textsuperscript{9} There is also evidence that hypercalcemia, gout and renal lithiasis are predisposing factors to pulp calcifications.\textsuperscript{10} The mechanism of apatite formation, also recognized as pathological biomineralization, behind dental pulp stone formation is hypothesized to be similar to joint calcifications, and renal calculi seen as the regressive changes observed in tissues as aging happens.\textsuperscript{11}

Kajander et al and Ciftcioglu et al also stated that bacteria known to produce biologic apatite over their cellular covering are responsible for dental pulp stone formations, just like renal calculi and other calcified tissues, leading to a hypothesis that this might be explained as a common factor between calcifications seen in the aging or traumatized pulp tissues and atheromatous plaques seen in the ischemic heart diseases (IHDs).\textsuperscript{12,13} Furthermore, osteopontin, a constituent of atherosclerotic plaque, apparently plays a role in plaque calcification, as it is produced by macrophages which, in turn, play a key role in the initiation of calcific changes seen in other necrotic tissues of the body as part of regressive, dystrophic changes attracting calcium, including the renal and carotid artery calcifications.\textsuperscript{14-16}

IHDs have been recorded as the leading cause of morbidity worldwide, wherein arteriosclerosis is the most common cause of IHDs, including stable and unstable angina, myocardial infarction (MI), cerebrovascular diseases such as stroke and peripheral artery disease (PAD), which is also known as peripheral vascular disease (PVD). The high prevalence and associated mortality of IHDs, thus, mandates the need for early markers that can help diagnose the condition at an early enough stage, so that preventive measures can be adopted before a frank clinical disease sets in.\textsuperscript{17}

Sufficient evidence exists in the literature which indicates that patients with IHDs show higher degree of pulp calcifications.\textsuperscript{18,19} Localized pulp calcifications are a normal part of the aging process of the tooth physiology, although pulp stones extending to the entire dentition, especially in younger age groups, are infrequent and need further evaluation to predict the risk of other associated diseases, including IHDs in the presence of compounding risk factors.\textsuperscript{20} The present study was planned to estimate the prevalence of pulp stones in patients diagnosed with/or undergoing treatment for IHDs.

Material and Methods

The present study consisted of 300 subjects within an age range of 25 to 65 years who were divided into two groups: study group consisting of 150 patients, including 113 males and 37 females, and 150 age- and sex-matched healthy controls. The control group consisted of subjects who had no significant medical history and in whom the risk of IHDs was ruled out on the basis of the absence of any predisposing risk factors, including a previous history of any chest discomfort or a positive family history for cardiovascular disease and related investigations, as per the cardiologist’s opinion, while patients who were either recently diagnosed with/or under treatment for IHDs were included in the study group. The patients who had a known history of other systemic illnesses including gout and renal disorders or, who were undergoing treatment for the same, had radiotherapy treatment in the past were excluded from the study. Furthermore, pregnant females and those who were unwilling to participate in the study were also excluded from the study, apart from subjects with possible dental causes of pulp stone formation, including subjects with crowns and bridges, extensive carious lesions or deeply placed restorations, subjects with history of orthodontic treatment, those afflicted with bruxism, and subjects who presented with severe attrition and previous history of trauma. The study protocol and its significance were explained in detail to each subject and a written, informed consent was obtained from all before their inclusion into the study. The structure and plan of the study was sent to the Ethics Committee of the Institution before the start of the study and their approval sought via. Institutional Ethics Committee Letter approval no SDDC/IEC/01–37–2019. Pulp stones were imaged using bitewing radiography (►Figs. 1 and 2) following conventional technique, while paralleling technique was used under standard conditions for standardization and reproducibility. The equipment used for taking bitewing radiographs was wall-mounted, very high-frequency DC (300 kHz), Carestream (Kodak) dental X-ray machine (Carestream Dental LLC, 3625 Cumberland Blvd. Ste. 700 Atlanta, GA) operating at 60 kVp tube voltage and 7 mA tube current, with a focal spot of 0.7 mm and focal length of 8 inches. The radiographic films used were Carestream (Kodak) E-Speed, size 2 dental films (31 mm into 41 mm), while an XCP-Rinn film holder (Dentsply DeTrey GmbH, De-Trey-Straße 1, 78467 Konstanz, Germany) was used for taking radiographs.

Evaluation of Bitewing Radiographs

All the radiographs were checked by three radiographers while the interexaminer variability was tested. The
Radiographs were examined using a magnifying glass in a darkened room, with the help of a light box, an even, diffuse light source, and peripheral light blocked to determine the presence of pulp chamber narrowing as well as pulp stones in the pulp chambers. Narrowing of pulp chamber was defined as a notable reduction in the size of pulp chamber, while pulp stones were identified as discrete, radiopaque masses inside the pulp chambers of the teeth and determined as present or absent. The results obtained were put to statistical analysis while interexaminer variability was ruled out through replicate observations in all samples.

**Statistical Analysis Used**
Statistical analysis was done using IBM SPSS Statistics for Windows version 21 (IBM Corp, Armonk, USA), while independent t-test and Chi-square test were used to check the prevalence of pulp stones in the study and control groups, based on their gender-, arch-, region- and side-wise distribution. \( p < 0.05 \) was considered statistically significant.

**Results**
The patients with IHDs exhibited 100% prevalence of pulp stones and the difference was found to be statistically significant (►Table 1), although there was a significant difference in the mean number of pulp stones observed in the study and control groups, with the study group revealing 2217 pulp stones against 639 pulp stones observed in the control group \( (p < 0.001) \) (►Table 2). Furthermore, no significant difference was found in relation to the gender predilection in both the groups (►Table 3). Again, although the results were not found to be statistically significant on comparison of the study and control groups, maxillary arch and posterior teeth were predominantly affected in both the groups (►Tables 4 and 5).

On analyzing the arch-wise prevalence of the total number of pulp stones in the study and control groups, there was a 51.33% involvement of the maxillary arch in the study group against 58.67% in the control group, while the prevalence of pulp stones was found to be 48.67% and 41.33% in case of mandibular arch in the study and control groups, respectively.

**Table 1** Number of subjects showing pulp stones in study and control groups

<table>
<thead>
<tr>
<th>Group</th>
<th>With pulp stone</th>
<th>%</th>
<th>Without pulp stone</th>
<th>%</th>
<th>Total</th>
<th>( \chi^2 )-Value</th>
<th>( p )-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study group</td>
<td>150</td>
<td>100.00</td>
<td>0</td>
<td>0.00</td>
<td>150</td>
<td>15.7890</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Control group</td>
<td>135</td>
<td>90.00</td>
<td>15</td>
<td>10.00</td>
<td>150</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>285</td>
<td>95.00</td>
<td>15</td>
<td>5.00</td>
<td>300</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2** Comparison of study and control groups with mean number of pulp stones by independent t-test

<table>
<thead>
<tr>
<th>Group</th>
<th>Number (%)</th>
<th>Mean</th>
<th>SD</th>
<th>t-Value</th>
<th>( p )-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study group</td>
<td>2217 (96.24%)</td>
<td>14.78</td>
<td>5.64</td>
<td>25.4998</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Control group</td>
<td>639 (27.59%)</td>
<td>4.26</td>
<td>1.06</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: SD, standard deviation.
The posterior teeth too showed a clear predilection for pulp stones, although the results were not found to be statistically significant when compared in relation to the study and control groups. On analyzing the region-wise prevalence of total number of pulp stones in the study and control groups, 87.33% of the posterior teeth were found to be afflicted with pulp stone formation against 12.67% in case of the anterior teeth. Similar results were obtained in the control group, wherein 86.00% of the posterior teeth revealed pulp stones on radiographic examination against the anterior teeth, which revealed a mere 14.00% prevalence of pulp stones in the control group. The results in relation to the predilection for the side of the jaw affected were found to be statistically insignificant in the present study ($p > 0.05$).

### Discussion

When pathological calcification occurs in nonviable tissues, it is known as dystrophic calcification, and it may occur despite normal serum levels of calcium. In contrast, the deposition of calcium salts in vital tissues is known as metastatic calcification, and it almost always reflects some degree of derangement in normal calcium metabolism, leading to hypercalcemia.\(^{21}\)

Dental pulp calcifications date back to the year 1921 when they were first mentioned by Norman and Johnson as dental pulp nodules, a term which was later modified to dental pulp stones or denticles.\(^{22}\) Pulp calcifications are usually reported as incidental findings on intraoral radiographs as discrete, radiopaque bodies enclosed within the pulp chambers or root canals, with a wide variation in the numbers seen.\(^{23}\)

Kronfeld and Boyle classified pulp stones histologically into true and false forms, wherein the true pulp stones are more irregular in shape and are lined by odontoblasts and thus composed of dentine, whereas false pulp stones are constituted by the degenerating cells of the pulp, which calcify as a part of the process of dystrophic calcification, attracting calcium despite normal serum levels.\(^{23-25}\) There is another category of pulp calcifications too, the diffuse or amorphous type which is seen in close association with the blood vessels.\(^{23}\)

Cardiologists have confirmed the role of calcium phosphate crystals in generating inflammation within the arteries and also playing a major role in acute MIs, leading to sudden death of the patients. The base of all calcifications including joint calcifications, renal calculi, atherosclerotic plaques, as well as pulp stones is made up of calcium phosphate crystals that elicit an acute immunological response as well as the eventual sequel, leading to widespread morbidity and mortality.\(^{11}\)

At the ultrastructural level, various studies on pulp stones have also reported similarity in the nature of pulp stones and calcifications observed in various other tissues in the body. Ninomiya et al found an even distribution of type I collagen throughout the pulp stones, while osteopontin was found to play an integral role in the process of calcification, as it was found in the peripheral areas of pulp stones.\(^{15}\) Likewise, Hirota et al also found similar occurrence of osteopontin in their immunohistochemical study on atherosclerotic plaque and urinary stones.\(^{26}\) The said observations from various

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Gender-wise prevalence of total number of pulp stones in study and control groups</th>
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<tbody>
<tr>
<td>Group</td>
<td>Males</td>
</tr>
<tr>
<td>---------</td>
<td>-------</td>
</tr>
<tr>
<td>Study group</td>
<td>113</td>
</tr>
<tr>
<td>Control group</td>
<td>109</td>
</tr>
<tr>
<td>Total</td>
<td>222</td>
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<table>
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<th>Table 4</th>
<th>Arch-wise prevalence of total number of pulp stones in study and control groups</th>
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<tbody>
<tr>
<td>Group</td>
<td>Maxillary arch</td>
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<td>---------</td>
<td>----------------</td>
</tr>
<tr>
<td>Study group</td>
<td>77</td>
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<tr>
<td>Control group</td>
<td>88</td>
</tr>
<tr>
<td>Total</td>
<td>165</td>
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<thead>
<tr>
<th>Table 5</th>
<th>Region-wise prevalence of total number of pulp stones in study and control groups</th>
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<tbody>
<tr>
<td>Group</td>
<td>Posterior region</td>
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<tr>
<td>---------</td>
<td>------------------</td>
</tr>
<tr>
<td>Study group</td>
<td>131</td>
</tr>
<tr>
<td>Control group</td>
<td>129</td>
</tr>
<tr>
<td>Total</td>
<td>260</td>
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<table>
<thead>
<tr>
<th>Table 6</th>
<th>Side-wise prevalence of total number of pulp stones in study and control groups</th>
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<tbody>
<tr>
<td>Group</td>
<td>Right side</td>
</tr>
<tr>
<td>---------</td>
<td>------------</td>
</tr>
<tr>
<td>Study group</td>
<td>74</td>
</tr>
<tr>
<td>Control group</td>
<td>77</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
</tr>
</tbody>
</table>
studies, thus, hypothesized a relationship between the occurrence of pulp stones and the calcifications observed in various other tissues of the body, including the arterial plaques as well as the renal calculi (nephrolithiasis), gall bladder stones (cholelithiasis), and various degenerative joint diseases (DJDs), proposing pulp stones to be a part of the systemic biominalization process affecting many tissues of the body.\textsuperscript{10,13,26-28}

Recently, it was also reported that calcified nanoparticles located in the cytolysosome could invade human dental pulp tissue through a receptor-mediated endocytosis and can be one of the important reasons behind dental pulp stone formation.\textsuperscript{13} Yang et al also detected vacuole containing these calcified nanoparticles, which indicated the cell's tendency for crystal deposits, inferring that the existence of calcified nanoparticles might promote calcification as crystallization of the nuclei leads to the formation of biogenic apatite structures.\textsuperscript{29} Similarly, Chen et al have also shown the relation of calcified nanoparticles/nanobacteria in the induction of renal calculi (nephrolithiasis).\textsuperscript{17} Zeng et al, too, elaborated the role of these calcifying nanoparticles (CNPs), also called nanobacteria, for pathological calcifications.\textsuperscript{31}

Furthermore, pulp stones vary in size, ranging from microscopic particles to large, discrete masses that almost completely obliterate the pulp chamber. Among them, only the larger pulp stones are radiographically apparent, while those that are either small in size or relatively less calcified and in the initial stages of calcification are not routinely detected by the conventional radiological procedures of diagnostics.\textsuperscript{16,28,32,33} Thus, the true prevalence of pulp stones is always likely to be a little higher than the results obtained from radiographic evaluations, although radiographs are considered to be the only means of evaluating the pulp stones in a noninvasive manner in the clinical settings.\textsuperscript{34}

The radiographic differentiation between pulp stone and pulpal sclerosis was demonstrated by Gauz and White who explained that early pulpal sclerosis is a degenerative process that precedes the formation of frank pulp stones and is not demonstrable radiographically, while diffuse pulpal sclerosis, on the other hand, produces a generalized calcification throughout a large area of pulp chamber or pulp canal.\textsuperscript{35} Pulp stones are discrete calcifications appearing within the pulp, which may be seen as a definite single or multiple radiopaque structures within the pulp chamber or canals. Similar results were obtained in the study conducted by Willman who examined 164 teeth from patients of different age groups and found a histological evidence of pulp calcifications in 87.2\% of the teeth examined against 14\% of the teeth wherein pulp stones could be detected radiographically.\textsuperscript{36}

Most of the prevalence studies have identified pulp stones using radiographic criteria in concordance with the one used in the present study. In the present study, it was found that pulp stones were prevalent in 100\% of the patients with IHDS in accordance with the study conducted by Ranjitkar et al who examined the prevalence of pulp stones in the Australian population and found the same in 46\% of the subjects and 10\% of the teeth examined in the study.\textsuperscript{34} Also, the said study observed subjects in the control group also to be afflicted with pulp stones similar to the findings of the present study, although the total number of pulp calcifications observed were lesser in number in the control group as compared with the study group.

Likewise, in relation to IHDS, Edds et al reported 74\% of the patients with IHDS to be afflicted with pulp stones, while Khojastepour et al reported 68.2\% of the patients with known cardiovascular diseases (CVD) and 28.2\% of subjects without CVD having pulp stones.\textsuperscript{7,9} Ezodzini-Ardakani et al, also, observed 67.3\% of the teeth in patients with IHDS having pulp calcifications.\textsuperscript{14} Nayak et al, although, recorded a little lesser prevalence of pulp stones in their study compared with these studies, confirming an increased prevalence of pulp stones in patients with known systemic diseases, primarily CVD, observing the prevalence of pulp stones in hypertensive patients to be 15.85\% higher than in the normal subjects included.\textsuperscript{8}

As far as the overall prevalence of pulp stones in the samples studied is concerned, al-Hadi Hamasha and Darwaze found pulp stones in 51\% of the radiographs and 22\% of the teeth examined in 814 Jordanian adults.\textsuperscript{33} Ravanshad et al also reported pulp stones in 46.9\% of the adult Iranian population included in their study.\textsuperscript{30} On similar lines, Sismen et al examined bitewing radiographs of 469 Turkish patients and found 57.6\% prevalence of pulp stones in the sample included and 15\% prevalence among the teeth examined.\textsuperscript{31} Likewise, Tamse et al evaluated full mouth radiograph of 300 patients and reported pulp stones in 20.7\% of the radiographs examined.\textsuperscript{38} Baghdady et al assessed 515 Iraqi subjects and recorded 19\% of the teeth with pulp stones.\textsuperscript{35} Similarly, Gulsahi et al, in their study, found pulp stones in 12\% of the subjects and 5\% of the teeth examined.\textsuperscript{39} Nayak et al, in a study on Indian population, examined 1432 teeth and found 9.35\% prevalence of pulp stones.\textsuperscript{8}

Contrary to the findings of these studies, Hill stated that of the subjects examined between 50 to 70 years, 66\% of the subjects exhibited pulp stones without a known evidence or history of other systemic diseases, similar to the finding of the study conducted by Khojastepour et al.\textsuperscript{37} The results of the present study also suggested an equal predisposition of both the sexes for the development of pulp stones, although few studies have reported a female preponderance toward the same and observed pulp stones to be more common in females than in males.\textsuperscript{34,38,41} Furthermore, Ranjitkar et al also suggested an increasing prevalence of pulp stones with age, a finding which was in accordance with the results obtained in the present study.\textsuperscript{34}

Also, both the groups in the present study showed a higher prevalence of pulp stones, wherein another notable finding in the present study was that in relation to the maxillary teeth, which seemed to have a definite predilection toward the development of pulp stones. The results of the present study revealed 51.33\% of maxillary teeth to be afflicted with pulp stones against 48.67\% of the mandibular teeth in the study group. Likewise, 58.67\% of the maxillary teeth were found to have pulp stones against 41.33\% of the mandibular teeth in the control group, showing a clear predilection of the maxillary teeth toward pulp stone formation against
the mandibular teeth. This was in accordance with the study conducted by Nayak et al who reported significantly higher number of pulp stones in the maxilla (12.36%) than in the mandible (5.95%) and in similar other studies conducted by Ranjitkar et al, Sisman et al and Turkal et al, who also confirmed similar findings with the results obtained from their studies.3,4,33

The present study also evidenced more number of pulp stones in the posterior teeth than anterior teeth, in accordance with the results of the studies conducted by Gulsahi et al, with around 87.33% of posterior teeth afflicted with pulp stones in the study group against 12.67% of the anterior teeth.45Similarly, in the control group, the corresponding values were 86.00% in case of posterior while 14.00% in case of anterior teeth, with a plausible explanation for this being the rich blood supply in the posterior teeth. al-Hadi Hamasha and Darwazeh had also put forth a hypothesis based on the observations made from their study that since posterior teeth were the largest, the rich blood supply in their pulp tissue would increase their probability for more calcifications observed.33

Thus, according to the results obtained in the present study, which were largely in line with the previous similar studies conducted in the past, the present study mandated for further studies to be conducted in line with the present study, so as to seek a definite correlation between the occurrence of pulp stones with other systemic diseases, as have been hypothesized to have a similar etiology behind the calcifications seen in them. Similar conclusions were drawn in the study conducted by Ozkalayci et al who had also suggested that a careful radiographic workup and a multidisciplinary approach in patients with an increased prevalence of pulp stones are of utmost significance to predict the possibility of other associated systemic disorders that might have predisposed the subjects to have this kind of a subtle change, seen in the pulp tissues, which is a less critically acclaimed clinical entity.43

Conclusions
The findings of the present study suggested a positive correlation between pulp stones and IHDs, highlighting the significance of dental radiographic examination, which may lead to the possible early detection of IHDs. Such a screening can easily be employed as a public health measure and further investigations planned, including a series of clinical and biochemical tests to rule out the risk for frank IHDs, perhaps, many years before the actual symptoms of vascular disease set in.

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Nil.

Conflicts of Interest
There are no conflicts of interest.

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