

## Original Article

# Clinical, radiological, and histological correlation in diagnosis of pulpitis

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## ABSTRACT

**Background:** To establish an endodontic diagnosis, a clinician should consider a variety of factors. Various studies have failed to demonstrate a strong correlation between histological findings with clinical and radiographic assessments. This study sought to evaluate the histopathological features of reversible and irreversible pulpitis diseases and their correlation with clinical diagnosis in extracted human molar teeth.

**Materials and Methods:** In this experimental *ex vivo* study, 75 molars with caries and three intact molars were used. According to the radiographic findings and clinical criteria and the need for root canal therapy, samples were categorized as having normal/reversible pulpitis and irreversible pulpitis. Immediately after extraction, an exposure was made at 2 mm below the cemento-enamel junction. Formalin-fixed specimens were decalcified, sectioned and stained with hematoxylin and eosin for histological examinations using light microscopy. Variables including the type and severity of the inflammation, hyperemia, necrosis, fibrosis and the existence of an odontoblastic layer and dentin bridge were evaluated. The Fisher's exact test and the Chi-squared test were used for statistical analysis.  $P < 0.05$  was considered as significant.

**Results:** Acute inflammation, hyperemia and pulp exposure were significantly more common among subjects with irreversible pulpitis ( $P < 0/005$ ). However, fibrosis was significantly higher in the reversible group ( $P < 0/005$ ). There were no statistically significant differences between the groups regarding the other variables.

**Conclusion:** Some discrepancies between clinical, radiographic and histological findings were observed in our experimental study. Indeed, effective clinical practice requires consideration of all discrepancies found.

**Key Words:** Diagnosis, histology, pulpitis, root canal therapy, signs and symptoms

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## INTRODUCTION

Dental caries is one of the most common infectious diseases found in humans. Providing a proper treatment plan for dental caries, especially at a young age, is a great asset to any practitioner. There are various therapeutic strategies along with a wide range of restorative materials for tooth decays.<sup>[1]</sup> Vital pulp therapy, as a biologic and conservative treatment modality, is one of the most effective treatments and is increasingly seen in permanent immature teeth and in teeth with closed apex.<sup>[2]</sup> Vital pulp therapy offers several further advantages over nonvital pulp therapies, including the maintenance of the tooth structure that contributes to increased mechanical resistance, as well as maintenance of defensive mechanisms provided by the vital pulp such as proprioception and tooth sensitivity.<sup>[3,4]</sup>

On the other hand, producing successful therapeutic outcomes in vital pulp therapies mainly depends on the accurate assessment of pulp status. Unfortunately, the diagnosis of pulpal pathology appears to be very complicated. There is no clear correlation among clinical signs and symptoms, pulpal sensibility tests, radiographic features, and the histological analysis of dental pulp.<sup>[5,6]</sup> To date, very few studies have directly investigated any correlations.<sup>[5-12]</sup> Therefore, the present study has been conducted to investigate the relationship between the histopathological status of the dental pulp tissues in carious teeth, with the clinical and radiographic features.

## MATERIALS AND METHODS

The present experimental study was approved by the Ethics Committee of Kerman University of Medical Sciences, Kerman, Iran (code: IR. KMU. REC1394.730). For the present study, seventy-five extracted mature carious molars, along with 3 intact ones, were used. The teeth were extracted from 83 patients ranging in age from 21 to 64 years old with an average age of  $35.7 \pm 10.88$ . Teeth were extracted from patients who refused to accept available treatment options, instead insisting on extraction for differing reasons such as financial constraints and dental fear. Teeth with calcified roots, resorption, previous root canal treatment, extensive restorations, crown, or severe periodontal problems were excluded. The practitioner provided periapical and bitewing radiographs prior to the extraction.

It is not appropriate to have an interval <6 months between radiographs.<sup>[13]</sup> However, we did not have access to some previous radiographs and in some cases the quality of radiographs were not acceptable. Hence, to avoid unnecessary radiation, patients who had radiographic examinations within the previous 6 months were excluded from the study. Patients who had radiographic examinations within the previous 6 months were also excluded from the study. According to the clinical criteria, the radiographic feature and the need for root canal treatment; and similar to the study by Ricucci *et al.*, samples were categorized as having normal/reversible pulpitis and irreversible pulpitis. Normal pulp was classified in the reversible pulpitis group because the pulp of both groups can be preserved.<sup>[9]</sup>

Patients in the normal/reversible pulpitis group did not have any history of overnight, throbbing, persistent, or prolonged pain, while they mostly reported a mild sensitivity to stimuli including cold, sweets or biting pressure. Moreover, pain from cold tests was not severe and did not linger more than 30 s. Percussion and palpation tests also proved negative. Radiographic examinations showed no pulp exposure and no periradicular destruction. A total of 27 teeth were placed in this group. In addition, 3 intact third molars were included in this group.

The group of patients with irreversible pulpitis reported severe pain to temperature changes that may or may not linger, spontaneous pain, referred pain and throbbing pains that resulted in patients waking up while proving difficult to control with painkillers. Eight teeth were tender to percussion. Moreover, palpation testing produced a sensitive response for 5 teeth. No periradicular changes were observed in radiographs, even though a few cases of periodontal ligament widening were found. Cases with radiographic exposure of the pulp were also included. A total of 48 teeth were placed in this group.

This study excluded cases other than those caused by dental caries. Cases in which clinical and radiographical factors were associated with pulp necrosis were also excluded from the study.

After recording the pulp response to the cold test by using a refrigerant spray (Denronic, Germany), a general practitioner performed all tooth extractions. The teeth were immediately cleaned with a flow amount of normal saline. To increase the penetration rate of the fixing agent and decreased risk of distortion

and cell lysis, pulp exposure was accomplished by use of a diamond fissure bur No. 012 L/837 (Tizkavan, Tehran, Iran) just beneath the cemento-enamel junction of an intact side of the teeth. Following fixation of the teeth in 10% buffered formalin for 24 h, all samples were decalcified in 15% nitric acid solution for 4–8 weeks (Merck/Germany). Subsequently, samples were washed in running tap water for 24 h and then dehydrated, embedded in paraffin and cut into serial sections of 3–5 microns.<sup>[14-16]</sup> Hematoxylin and eosin-stained slides were examined under a light microscope (Olympus, Tokyo, Japan) with  $\times 10$  and  $\times 40$  magnifications. The pathologist scanned different areas of the pulpal tissue and the worst pattern was recorded for each sample.<sup>[17]</sup> The following features were assessed: The type and severity of inflammation, hyperemia, necrosis, fibrosis and the presence of an odontoblastic layer and dentin bridge. The histological sections were given scores as previously described with minor modifications [Table 1].<sup>[15,18]</sup> Reproducibility was determined using the Kappa (K) coefficient. K coefficients were  $\leq 0.76$  for all items.

The X-ray diagnosis was performed by an endodontist under  $\times 2.5$  magnification on a negatoscope. The occurrence of pulp exposure was recorded. The kappa value for the intra-examiner reliability was 0.82, indicating almost perfect agreement between the two measurements.

Statistical analysis included measures of central tendency and dispersion. Data were also analyzed by Chi square and Fisher's exact test using the SPSS software, version 16 (SPSS, Inc., Chicago, IL, USA).

## RESULTS

Table 1 represents the histopathological scoring system used for the present study.

The type of inflammation, hyperemia and fibrosis were significantly different between the two comparison groups [Table 2]. 20.8% of the teeth with irreversible pulpitis showed acute inflammation. However, 43.3% of the specimens with reversible pulpitis showed no inflammation (Fisher exact test,  $P = 0.005$ ). In the reversible pulpitis group, 13.3% of the samples exhibited severe hyperemia, whereas 47.9% of the teeth with irreversible pulpitis showed severe hyperemia (Chi-square test,  $P = 0.006$ ). Moreover, 63.3% of teeth diagnosed with reversible pulpitis presented fibrosis, while in the irreversible group, only 27.1% of the samples had fibrosis (Chi-square test,  $P = 0.002$ ). In 58.3% of the cases in the irreversible group, pulp exposure could be detected on radiographs, while none of the specimen in the reversible pulpitis group exhibited pulp exposure (Chi-square test,  $P = 0.0001$ ).

There were no significant differences between the two groups with respect to the severity of inflammation, necrosis, and presence of an adjacent odontoblastic layer [Table 3]. Most of the cases in both groups showed mild inflammation. In the reversible pulpitis group focal necrosis was observed in one case, while in the irreversible group, 14.6% showed focal necrosis ( $P > 0.05$ ). An odontoblastic cell layer was present in 96.7% of the teeth diagnosed with reversible pulpitis and in 87.5% of the samples of irreversible pulpitis group ( $P > 0.05$ ) [Figure 1]. Moreover, we didn't observe dentin bridge formation

**Table 1: Scoring system used for histopathologic evaluation of the pulp**

Variable	0	1	2	3
Inflammation type	No inflammation	Acute inflammation (neutrophils)	Chronic inflammation (lymphocyte and plasmacells)	A combination of acute and chronic inflammation
Inflammation severity	No inflammation	Mild (<30 inflammatory cells)	Moderate (30-60 inflammatory cells)	Severe (>60 inflammatory cells)
Hyperemia	<3 blood vessels	3-5 blood vessels	More than 5 blood vessels	
Necrosis	No necrosis	Focal necrosis		
Fibrosis	Fibrosis -	Fibrosis +		
Location of dentin bridge	No dentinal bridge formation	Presence of dentinal bridge besides the lesion	Presence of dentinal bridge connected to the lesion	
Dentin bridge quality	Dentinal bridge without tunnel defects	Dentinal bridge with tunnel defects	No dentinal bridge formation	
Presence of adjacent odontoblast layer	-	+		
Pulp exposure in radiographic evaluation	-	+		

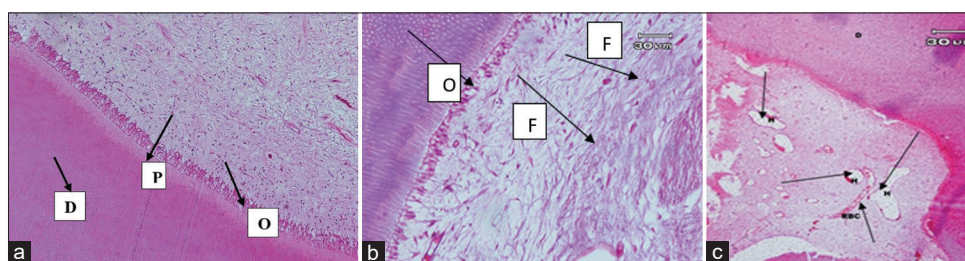
**Table 2: The variables with significant differences in scores between the groups**

Variable	Inflammation type*					Hyperemia**				Fibrosis***		
	0	1	2	3	Total	0	1	2	Total	0	1	Total
Reversible pulpitis, <i>n</i> (%)	13 (43.3)	0	14 (46.7)	3 (10)	30 (100)	6 (20)	20 (66.7)	4 (13.3)	30 (100)	11 (36.7)	19 (63.3)	30 (100)
Irreversible pulpitis, <i>n</i> (%)	8 (16.7)	10 (20.8)	21 (43.8)	9 (18.8)	48 (100)	8 (16.7)	17 (35.4)	23 (47.9)	48 (100)	35 (72.9)	13 (27.1)	48 (100)

\*\**P*=0.006 Chi-square test; \*\*\**P*=0.002 Chi-square test. *P*=0.005 Fisher test

**Table 3: The variables with no significant differences in scores between the groups**

Variable	Severity of inflammation					Necrosis			Presence of an adjacent odontoblastic layer		
	0	1	2	3	Total	0	1	Total	0	1	Total
Reversible pulpitis, <i>n</i> (%)	12 (40)	16 (53.3)	1 (3.3)	1 (3.3)	30 (100)	29 (96.7)	1 (3.3)	30 (100)	1 (3.3)	29 (96.7)	30 (100)
Irreversible pulpitis, <i>n</i> (%)	8 (16.7)	32 (66.7)	5 (10.4)	3 (6.2)	48 (100)	41 (85.4)	7 (14.6)	48 (100)	6 (12.5)	42 (87.5)	48 (100)



**Figure 1:** Hematoxylin and eosin stained demineralized sections of extracted carious molars. (a) Normal dentine-pulp showing: D: Dentine; P: Predentin layer; O: Odontoblast cell layer; (x40). (b) Histological features of reversible pulpitis in the area adjacent the caries site: D: Dentine; O: Odontoblast cell layer; F: Fibrosis. (c). Histological features near the carious lesion in tooth section with irreversible pulpitis: D: Dentine; H: Severe hyperemia.

adjacent to the carious lesion in any of the samples examined.

There were significant differences between reversible and irreversible pulpitis groups regarding the responses to the cold test (*P* < 0.001). In the irreversible pulpitis group, 64.6% of the patients experienced pain for <10 s. While, 29.2% of the cases felt a pain lasting more than 10s by the cold stimulation. Among the samples of this group, 6.3% reported no pain following the cold test. In the reversible pulpitis group, 96.7% of the cases had 1–10s pain sensation due to the cold stimulation of the teeth. Notably, there were no cases of having pain for more than 10s. In 3.3% of the cases cold stimulation didn't elicit dental pain.

Histological examination of intact pulps revealed uninfamed connective tissues, with abundant cells, neurovascular bundles, and cell layer of odontoblasts.

## DISCUSSION

In the present study, the number of noninflamed samples was significantly higher in the reversible pulpitis group than the irreversible one. Moreover,

acute inflammation was more frequent in irreversible pulpitis compared to the other group. Irreversible pulpitis is characterized by the presence of bacteria or their by-products in dental tubules and the pulp tissue adjacent to deep caries;<sup>[19]</sup> as well as through an acute-inflammatory reaction predominantly characterized by the presence of neutrophils in the tissue beneath a lesion, suggesting neutrophil-chemotactic activity.<sup>[20]</sup>

Nonetheless, no significant difference was observed between the two study groups regarding the severity of inflammation. Mejare *et al.*, in a systematic review, stated that there is not enough evidence to determine an association between the presence, nature and duration of clinical symptoms, with pulp inflammation severity.<sup>[21]</sup> The presence of inflammatory cells in a reversible pulpitis condition is not a strange finding. The inflammatory mechanisms help with pathogen elimination and repair stimulation. IL-10 is an immunosuppressive cytokine produced by many immune and non-immune cells, acting to suppress inflammation-associated immune responses, thus limiting damage to the host.<sup>[22]</sup> Moreover, within an inflammatory process, TNF- $\alpha$  may activate the p38

mitogen-activated protein kinase pathway, and induce odontoblast-like cell differentiation into dental pulp stem cells by increasing dentin sialoprotein, as well as dentin phosphoprotein expression, in turn forming tertiary dentin.<sup>[23]</sup> The accurate measurement of these cytokines may help predict the long-term prognosis of direct pulp capping. Besides, some molecular markers of inflammation from the dentinal fluids may also prove indicative of pulpal inflammation.<sup>[24]</sup>

Varying degrees of pulp inflammation have been found when caries extend through dentin, and more than half the distance to the pulp. Interestingly, in the cases where caries involve more than 50% of the dentin thickness, the severity of pulpal inflammation in primary molars is less in occlusal decays than in proximal ones.<sup>[16,25]</sup> Further investigation into the assessment of pulpal inflammatory changes in permanent teeth, in conjunction with the location of carious lesions, is recommended.

Here, the presence of severe hyperemia was significantly more likely in the irreversible pulpitis group than in the reversible pulpitis one. However, in a pulp hyperemic condition, only some slight changes in an odontoblastic layer without inflammatory cells are typically observed.<sup>[17]</sup> Within the present study, in accordance with some previous studies,<sup>[26,27]</sup> hyperemia was assessed based on the number of blood vessels. Nevertheless, we contend that immunohistochemical staining based on the vascular markers would be a more accurate method for assessment of vascular changes.

One of the interesting findings in our study was the high incidence of fibrosis in the reversible pulpitis group. Different inflammatory cytokines including interleukin-10 (IL-10) were detected in the dental pulp beneath both deep and shallow carious lesions.<sup>[28,29]</sup> Elsalhi *et al.* showed significantly higher levels of IL-10 in the pulps of asymptomatic deep carious teeth as compared to the samples with irreversible pulpitis.<sup>[30]</sup> The role of IL-10 in contributing to the pathophysiologic development of fibrosis has been already suggested. Sun *et al.*, indicated that IL-10-induced fibrocyte recruitment is likely mediated by the CCL2-CCR2 axis.<sup>[31]</sup> Moreover, dental pulp undergoes numerous regressive and reactive changes as individual ages. Increased fibrosis is one of the microscopically evident alterations.<sup>[32]</sup>

In the irreversible pulpitis group, 41.7% of the samples showed pulp exposure. In the study by Hasler

and Mitchell, the rate of inflammation in nonexposed samples was significantly less than that of the exposed ones. However, it's an old study with wide confidence intervals and small sample size.<sup>[33]</sup>

In the present study, one case of the reversible pulpitis group exhibited localized necrosis. In a recent study, Zanini *et al.* also mentioned that pulp necrosis may be seen in asymptomatic patients whose disease could be wrongly diagnosed as reversible inflammation.<sup>[11]</sup> Decision making for a treatment plan would be even more complicated when we see good treatment outcomes resulting from vital pulp therapy techniques on symptomatic permanent teeth.<sup>[4]</sup>

If the carious process is controlled or arrested, stem/progenitor cells within the pulp congregate at the site of injury and to differentiate into odontoblast-like cells. These cells deposit a tertiary reparative dentin matrix, which clinically results in dentin bridge formation.<sup>[22]</sup> In the present study, probably due to the presence of active carious lesions, we didn't observe dentin bridge formation adjacent to the lesion in any of the samples examined. However, a dentin bridge is not necessarily a criterion for the healing of the pulp.<sup>[34]</sup>

Here, there was only 1 case of the reversible pulpitis group in which odontoblast layer could not be identified. However, the patient was 62 years old and thus we believe this finding may be attributable to the age of the patient. Beneath the carious lesion, primary odontoblasts would be exposed to bacteria, and their by-products which negatively affect them.<sup>[35]</sup> Cellular senescence may also occur in dental pulp tissue by different cell death pathways including necrosis, apoptosis or nonapoptotic pathways such as necroptosis, pyroptosis, or nemosis.<sup>[36,37]</sup>

In this study, 29.2% of the samples in the irreversible pulpitis group had a reaction longer than 10 s following a cold testing, while none of the cases with reversible pulpitis had lingering pain. Hyman and Cohen stated that endodontic diagnostic tests could adequately identify cases which were free of disease, but were less effective in identifying disease-positive persons. The authors therefore suggested that practitioners should be prudent in their diagnosis of irreversible pulpal disease.<sup>[38]</sup> Interestingly, Ricucci *et al.* concluded that there is a good correlation between clinical and histological findings, especially in cases of normal pulp/reversible pulpitis.<sup>[9]</sup> In a systematic review, Mejare *et al.* found that the overall

evidence was insufficient to assess the value of pulp testing, with reference to heat/cold stimulation in identifying the pulp condition.<sup>[21]</sup> Molecular-based strategies hold significant promise and may end up proving relevant in making the best treatment plan based on the pulp conditions.<sup>[11]</sup>

Among the limitations of this study, the followings is worthy of note. For histological studies, teeth should be extracted. Because most patients who are referred for tooth extraction have advanced carious lesions, the number of irreversible pulpitis samples in this study was therefore more than the samples with reversible pulpitis. Moreover, pulp inflammation involves several biological processes that can be evaluated at the macroscopic, microscopic, and molecular levels, and it is therefore imprecise to over-speculate on the nature of the cells, as well as the conditions of pulp tissue, when considering solely a morphological observation at the level of light microscopy.

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### Conflicts of interest

The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or nonfinancial in this article.

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