Original Article - Evaluative Study

Histopathological Evaluation of Dental Follicle Associated with Radiographically Normal Impacted Mandibular Third Molars

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Abstract

Introduction: Removal of impacted mandibular third molar is a common procedure performed in oral surgery. Indications for removal of the third molar have generated much discussion in dentistry. The presence of pericoronal pathosis is generally accepted reason for the extraction of impacted mandibular third molars. Radiographic pathology is usually defined as a pericoronal radiolucency measuring about 2.5 mm or larger in any dimension. **Purpose:** This study aims to evaluate the histopathologic changes in radiographically normal dental follicles associated with impacted mandibular third molars. **Methods:** After extraction of 50 impacted mandibular third molars, dental follicle associated with extracted teeth was placed in 10% formalin solution. Histopathologic examination was done. The type of pathological changes was recorded based on histopathological reports. Patients' gender, age, and radiographic parameters were recorded. **Results:** Cystic changes were found in 24% of radiographically normal impacted mandibular third molars. Significant cystic changes were observed in position A vertically impacted lower third molars (ILTMs). Male predominance for cystic change was seen with a male–female ratio of 2:1. **Conclusion:** The result of the present study shows that radiographic analysis may not be reliable technique for the diagnosis of cystic changes in ILTM. The presence of cystic changes can be found even in radiographically normal impacted mandibular third molars. Hence, we recommend that impacted mandibular third molars should be removed and histopathological analysis should be conducted on all surgically extracted dental follicles.

Keywords: Dental follicle, impacted lower third molar, pericoronal pathology, pericoronal radiolucency

Introduction

Mandibular third molars are regarded as the most commonly impacted teeth in the oral cavity.[1] Removal of impacted mandibular third molar is a common procedure performed in oral surgery.[2] Some clinicians suggest prophylactic removal before development of pathologic changes, while others propose observation and periodic monitoring. However, the presence of pericoronal pathosis is a generally accepted reason for the extraction in their case. A radiographic pathology is defined as a pericoronal radiolucency measuring about 2.5 mm or larger in any dimension. Radiographically, the dental follicles of the impacted teeth present as a slight semicircular radiolucency around unerupted teeth.[3] It is often assumed that the absence of pericoronal radiolucency reflects the absence of pathosis.[4]

The decision of removing an impacted tooth is often less challenging when signs and symptoms of pathosis are present but is made more demanding when the patient is asymptomatic.[5] In 1979, the National Institutes of Health Consensus Development Conference agreed on indications for removal of impacted third molars, including infection, nonrestorable carious lesions, cyst, tumor, and destruction of adjacent tooth and bone.[6] One conclusion of the conference was that well-defined prospective studies are needed to determine, what to do about asymptomatic teeth?[7]

According to Osaki *et al*., retained wisdom teeth may cause infection in elderly patients. It was proposed that removing these impacted wisdom teeth in a younger subject might be a

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preventive measure for probable lesions in adulthood. On the other hand, Stephen reported that the risk of a retained impacted third molar is over exaggerated and their removal to be done only in case of a definitive pathology. In a 12 year followup study conducted by Alquist and Grondahi, it was revealed that minor changes occur in 15% of the impacted teeth.[3]

Rakprasitkul suggested that impacted third molars should be extracted before pathologic changes develop in their pericoronal tissue and be routinely removed in individuals over the age of 20 years.[5]

Knight *et al*. looked at the prevalence of dentigerous cyst and found that 44.7% of 170 impacted teeth examined had associated dentigerous cyst, some with little or no radiographic evidence of pathology. Manganaro reported that 45.5% of dentigerous cysts associated with 100 impacted third molars showed little or no radiographic evidence of pathosis.

Numerous justifications against and for prophylactic extraction of asymptomatic impacted third molar have been offered in the past leading to confusion in the minds of practitioners.[6] Numerous studies with conflicting results have been conducted on potential of follicular tissues to undergo pathological alteration.[8] Hence, this study aims to evaluate the histopathologic changes in radiographically normal dental follicle associated with impacted mandibular third molars.

Methods

This study was done on patients requiring removal of mandibular third molar under local anesthesia, who reported to the department of oral and maxillofacial surgery. The follicle associated with 50 impacted lower third molars (ILTMs) was included in this study. Third molar position was assessed using Pell and Gregory classification.

Patients' gender and age were recorded. Healthy patients in the age group of 17–50 years having impacted third molar with pericoronal radiolucency of 2.4 mm or <2.4 mm were included in the study. Impacted third molar with pericoronal radiolucency >2.4 mm, pregnant and lactating females, patients with a history of allergy to lignocaine, and medically compromised patients were excluded from the study. Under standard aseptic conditions, ILTM was surgically removed. Dental follicle either came out along with tooth or remained in the socket, and curette was used to remove dental follicle from socket. It was immediately fixed in 10% formalin and sent to the department of oral pathology for further processing and staining. Histological evaluations of all the samples were done in the department of oral pathology under light microscope [Figures 1 and 2].

The features evaluated histopathologically were as follows:

1. Presence of epithelial tissue
2. Type of epithelial tissue
    a. Reduced enamel epithelium (REE)
    b. Stratified squamous epithelium (SSE)
3. Type of connective tissue (CT)
    a. Loose fibrous
    b. Dense fibrous.

Dental follicular tissue showed the presence of REE, and loose fibrous CT is regarded as normal dental follicle in this study. Any dental follicle which showed the presence of SSE and dense fibrous CT is regarded as cyst. The histopathological criteria, which are used to differentiate between dental follicle and cystic changes in the current study, are based on the studies conducted by Saravana and Subhashraj,[1] Baykul *et al*.,[2] Adelsperger *et al*.,[4] and Simşek-Kaya *et al*.[9] [Figures 3 and 4].

Results

Fifty ILTMs were extracted and dental follicles attached to it were subjected to histopathological evaluation. Radiographic findings were correlated for each patient with the histologic findings, and the data were analyzed for association with age, gender, angular position, and depth of tooth. The age range of patients was 17–50 years with mean age being 26.26 years. Of the total 50 patients, 34 (68%) were male and 16 (32%) were female. Out of 50 ILTM, 23 (46%) teeth were found in the right side of the mandible and 27 (54%) on the left side. Patients were divided into two groups according to the size of pericoronal radiolucency. Fifteen patients were in the size range of 1.7–2 mm and 35 patients were in size range of 2.1–2.4 mm. Depth of tooth was measured according to Pell and Gregory classification. Of the total number of patients, 22 (44%) showed position A and 28 (56%) showed position B. Nineteen (38%) patients showed mesioangular impacted tooth, 13 (26%) were vertical, 9 (18%) were horizontal, and 9 (18%) were distoangular tooth [Table 1].

Forty-five (90%) specimen showed the presence of epithelium and only 5 (10%) specimens were devoid of epithelium. Of the 45 follicles with epithelium, 31 (68.9%) showed REE and 14 (31.1%) showed SSE. Twenty-seven (54%) patients showed loose fibrous CT, and dense fibrous CT was found in 23 (46%) patients. Histologically, inflammation was present in 34 (68%) cases and was absent in 16 (32%) cases. Ten (20%) patients showed the presence of odontogenic rests [Table 2]. Cystic changes were absent in 38 (76%) patients and cystic changes were found in 12 (24%) patients. The presence of cystic changes in mesioangular, vertical, horizontal, and distoangular impaction was 2 (16.7%), 4 (33.3%), 3 (25%), and 3 (25%), respectively. Nine (75%) impactions showed cystic changes in position A ILTM. Three (25%) impactions showed cystic changes in position B. Significant relation was observed between cystic changes and depth of tooth. Cystic changes was found in 11 (91.7%) patients with pericoronal radiolucency measuring between 2.1 and 2.4 mm. Eight (66.7%) cystic changes were found in the right side of ILTM [Table 1]. Inflammation was found in 6 (50%) cystic cases. Odontogenic rests are found in only 1 (8.3%) cystic case. Cystic change was found in 8 (66.7%) male and 4 (33.3%) female patients and hence showed male predominance. Cystic change showed male-to-female ratio of 2:1 [Table 2].

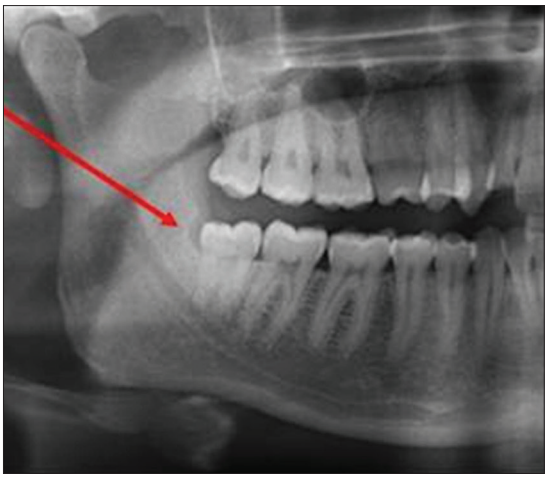

Figure 1: Vertical impacted lower third molar (cropped orthopantomography)

Figure 2: Dental follicle attached with extracted tooth

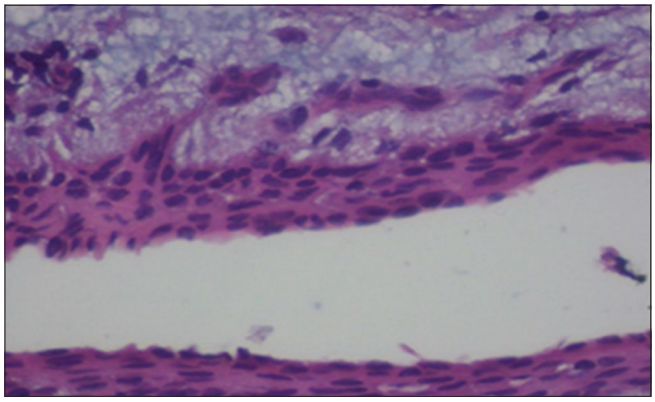

Figure 3: Histopathological appearance of normal follicle (reduced enamel epithelium + loose connective tissue)

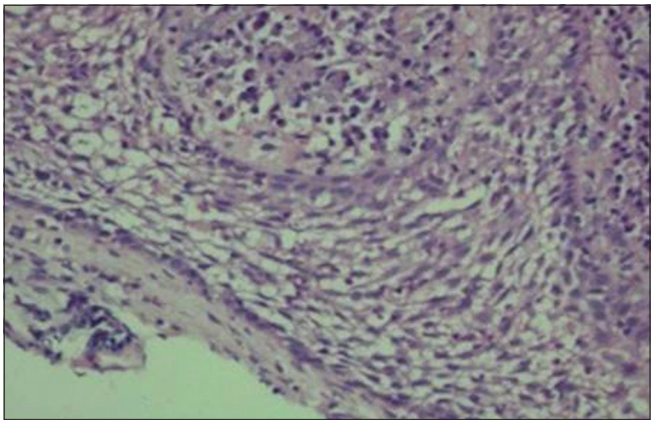

Figure 4: Histopathological appearance of cystic changes (stratified squamous epithelium + dense connective tissue)

Discussion

Removal of impacted mandibular third molars is a common procedure performed by dentists and oral surgeons.[2] The presence of disease associated with third molar is an indication for their removal; prophylactic removal remains controversial. Currently, there is a little scientific evidence to support routine removal of ILTM for prevention of disease.[9] Previous literature suggests that pericoronal radiolucency of smaller than 2.5 mm in width is nonpathologic.[8] There are studies which report pathologic changes in radiographically normal ILTMs. Unlike previous studies which were done on the cases in which clinical signs and symptoms were absent (asymptomatic), the present study analyzed the pathological changes in both symptomatic and asymptomatic cases. The follicular sac surrounding a tooth is interpreted in a radiograph as pericoronal radiolucency, the width of which is of high importance to differentiate between a normal and abnormal dental follicle.[1] Stephens *et al*. pointed out the probability of cyst with pericoronal space >2.5 mm. According to Glosser and Campbell, the radiographic pathology was defined as pericoronal radiolucency of 2.5 mm or more.[10] Saravana and Subhashraj quoted Conklin and Stafne study which found relation between width of pericoronal space and presence of epithelial lining associated with impacted tooth.[1] Many studies had shown pericoronal radiolucency of >2.5 mm to be considered as a "radiographic pathology," therefore in our study, patients with pericoronal radiolucency of 2.4 mm

Table 1: Correlation of Radiographic Parameters with cyst

Radiographic parameters	Cyst		*P*
	Absent (*n*=38)	Present (*n*=12)	
Angulations tooth			
Mesioangular	17 (44.7%)	2 (16.7%)	0.339
Vertical	9 (23.7%)	4 (33.3%)	
Horizontal	6 (15.8%)	3 (25%)	
Distoangular	6 (15.8%)	3 (25%)	
Depth of tooth			
Position A	13 (34.2%)	9 (75%)	0.013*
Position B	25 (65.8%)	3 (25%)	
Side of tooth			
Right	15 (39.5%)	8 (66.7%)	0.099+
Left	23 (60.5%)	4 (33.3%)	
Size of radiolucency			
1.7-2.0 mm	14 (36.8%)	1 (8.3%)	0.060+
2.1-2.4 mm	24 (63.2%)	11 (91.7%)	

Table 2: Correlation of Histopathological parameters with cyst

Histopathological parameters	Cyst		*P*
	Absent (*n*=38)	Present (*n*=12)	
Epithelium			
Absent	5 (13.2%)	0 (0%)	0.319
Present	33 (86.8%)	12 (100%)	
Type of epithelium			
REE	31 (81.6%)	0 (0%)	<0.001**
SSE	2 (5.3%)	12 (100%)	
Type of CT			
Loose fibrous	27 (71.1%)	0 (0%)	<0.001**
Dense fibrous	11 (28.9%)	12 (100%)	
Inflammation			
Absent	10 (26.3%)	6 (50%)	0.125
Present	28 (73.7%)	6 (50%)	
Odontogenic rest			
Absent	29 (76.3%)	11 (91.7%)	0.246
Present	9 (23.7%)	1 (8.3%)	

were chosen. Adelsperger *et al*. suggested that the absence of radiographic disease is not necessarily reflective of the absence of disease.[4] Osaki *et al*. proposed that removing impacted third molar teeth in younger people might be considered a preventive measure for the probable lesions in the adulthood. On the other hand, Stefen stated that the risk of retained impacted third molar has been exaggerated and suggested that their extraction should be only performed if the definitive pathologic entity is found.[11]

There are no widely accepted criteria for separating dental follicle and cyst, which remain an area of controversy.[12] In the present study, any dental follicle showing the presence of SSE and dense fibrous CT is regarded as cystic. Adelsperger *et al*. considered the presence of squamous metaplasia in follicle lining as cystic changes.[4] In Baykul *et al*. study, any soft-tissue specimen with the presence of dense fibrous CT wall lined by few layers of SSE was defined as cystic.[2] In Simşek-Kaya *et al*. study, specimens were classified as cystic if they showed a dense fibrous CT wall lined with several layers of SSE.[9] In Saravana and Subhashraj study, the presence of SSE lining of dental follicle was suggestive of dentigerous cyst and lack of SSE lining of dental follicle, indicative of normal dental follicle.[1] Varying criteria for the diagnosis of dental cyst have been described. Godoy *et al*. adopted the following histopathological criteria for the diagnosis of a cystic lesion such as observation of thin SSE lining of cystic cavity and exhibiting area of continuity and are arranged throughout a connective capsule of variable density. The criteria for dental follicle included observation of thin and discontinuous simple cuboidal cells of REE, along with loose fibrous CT capsule.[12] Some studies suggested that squamous metaplasia in pericoronal tissues of impacted teeth is related to normal changes that occur during aging while others believe this metaplasia to be an early pathologic event in dental follicle, possibly leading to cyst formation.[4] This study found cystic changes in 12 (24%) of impacted third molar teeth that were radiographically normal. Glosser and Campbell found cystic changes in 37% of ILTMs.[10] Baykul *et al*. study showed 50% cystic changes.[2] Güven *et al*. showed incidence of cyst formation in 2.3% of cases.[13] Saravana and Subhashraj reported incidence of cystic changes in 46% of cases.[1] Yildirim *et al*. found that 23% of follicles showed cystic changes. Adelsperger *et al*. found that 34% of samples in their study exhibit squamous metaplasia indistinguishable from histologic changes found in dentigerous cyst.[4] Yadav *et al*. study showed pathologic changes in 4.44% of follicular tissues.[3] Radiographic studies have suggested that routine removal of the third molar for prevention of disease may not always be necessary, but that data may be skewed by removal of most of diseased teeth at relatively early age, leaving fewer cases of disease to be diagnosed at later age. It is also possible that at least some of these cystic areas involute or do not progress to become larger destructive lesions.[10] Several explanations are possible for the difference in cyst incidence reported in various studies. The need for surgical enucleation can be eliminated if spontaneous cyst involution could occur over time. The tissue could undergo conversion to quiescent state, persisting only as a histologic aberration of little clinical significance. Difference in perception of requirement for the diagnosis of dentigerous cyst may determine which soft tissues are deemed "cystic."[4]

This study found 58.3% of cystic changes among patients older than 24 years. Yildirim *et al*. found that 89% of patients whose follicles showed cystic changes were >20 years.[14] Simşek-Kaya *et al*. found that 80% of cystic changes and 58.06% of inflammations occurred in patients aged 20–24 years. Simşek-Kaya *et al*. finding of higher incidence of pathological changes among patients under the age of 25 years conflicts with their finding that the likelihood of cystic changes is independent of tooth development.[9] Baykul *et al*. found that 56% of patients older than 20 years showed cystic changes and most of them occurred between 20 and 25 years. Therefore, age may be used as an indication for removing ILTM surgically, as the risk of surgical morbidity increases with increasing age.[2] In this study, 84.6% of ILTMs showed pericoronal radiolucency between 2.1 and 2.4 mm in the age group of 25–29 years and 30 years and above. We found that size of pericoronal radiolucency increases with age [Table 3]. About 91.7% of cystic changes were found in follicles with radiolucency 2.1–2.4 mm.

This study found male predominance for cystic changes. Eight out of 12 cases of cystic changes were found in males.

The histopathological diagnosis of cystic changes showed a male-to-female ratio of 1.3:1 in a study done by Baykul *et al*.[2] In Adelsperger *et al*. study, histologic diagnosis of dentigerous cyst showed male-to-female ratio of 1.5:1.[4] Saravana and Subhashraj found male-to-female ratio being

Table 3: Correlation of radiographic parameters with age

Radiographic parameters	Age in years			*P*
	18-24 yrs (*n*=24)	25-29 yrs (*n*=13)	30 & above (*n*=13)	
Angulations tooth				
Mesioangular	11 (45.8%)	5 (38.5%)	3 (23.1%)	0.162
Vertical	3 (12.5%)	6 (46.2%)	4 (30.8%)	
Horizontal	5 (20.8%)	0 (0%)	4 (30.8%)	
Distoangular	5 (20.8%)	2 (15.4%)	2 (15.4%)	
Depth of tooth				
Position A	7 (29.2%)	5 (38.5%)	10 (76.9%)	0.017*
Position B	17 (70.8%)	8 (61.5%)	3 (23.1%)	
Side of tooth				
Right	11 (45.8%)	5 (38.5%)	7 (53.8%)	0.715
Left	13 (54.2%)	8 (61.5%)	6 (46.2%)	
Size of radiolucency				
1.7-2.0 mm	11 (45.8%)	2 (15.4%)	2 (15.4%)	0.065+
2.1-2.4 mm	13 (54.2%)	11 (84.6%)	11 (84.6%)	

1.7:1.1. Daley and Wysocki reported the male predominance for cystic changes and suggested that this may be due to the prophylactic extraction of third molars due to the smaller jaw size in female patients.[2] Angular position of ILTM was also evaluated in this study. In this study, 4 (33.3%) cases of cystic changes were found in vertical ILTM followed by 3 (25%) cases each in horizontal and distoangular ILTM. Studies by Simşek-Kaya *et al*. and Yildirim *et al*. had stated that vertical and mesioangular molar showed greater tendency toward pathological changes.[9,14] Knutsson *et al*., in their study, reported higher incidence of cystic changes in horizontal ILTM.[15] Eliasson and Heimdahl reported higher incidence of pathologic changes in horizontal impacted third molar. Baykul *et al*. found higher incidence of cystic changes in vertically position ILTM, followed by horizontal and mesioangular positions.[2] Baykul *et al*. and Yildirim *et al*. included only fully impacted teeth in their study, so this may be reason of higher incidence of cystic changes in vertical ILTM in their study.[2] This study found statistically significant relation between cystic changes and depth of impacted tooth. Nine (75%) of cystic changes were found in position A impacted tooth. Werkmester *et al*. and Simşek-Kaya *et al*. found strong correlation between depth of impaction and prevalence of pathological changes in dental follicle.[9] In this study, 8 (66.7%) cases of cystic changes were found in the right side. Adelsperger *et al*. found no predilection for specific anatomic site of cyst occurrence (left or right).[4] Mesgarzadeh *et al*. found more ILTM on the left side than the right.[16]

In this study, 84% of cases showed inflammation of dental follicle in the age group of 24–29 years while 61.5% of cases showed inflammation in the age group of 30 years and above. Higher incidence of inflammation was found in the age group of 25–29 years and 30 years and above, as compared to the age group of 18–24 years. This study does not show any significant relationship between age and inflammation of dental follicle. Khorasani and Samiezadeh found significant relationship between age and inflammation of dental follicle. It seems that longer these structures remain in the bone, larger the possibility of inflammatory reaction within CT. Various factors including previous periodontal abscess, second molar pericoronitis, or a physiologic alveolar bone resorption may be a cause of this event. In addition, with increasing age, physiologic alveolar bone resorption occurs, which can gradually expose the once completely impacted third molar to oral cavity and subsequently lead to an increase risk of infection.[11] Yadav *et al*. found a significant relationship between increase in patients age and inflammation of dental follicle. It seems that the longer the follicular tissue remains in bone, larger the possibility of an inflammatory reaction within CT.[3] In this study, 8 (23%) cases of inflammation of dental follicle showed SSE. Khorasani and Samiezadeh found a significant relationship between nonspecific chronic inflammation and presence of SSE. It could be postulated that inflammation may act as stimulator on the lining epithelium of dental follicle and changes it from its normal cuboidal REE form to squamous type, which is more resistant to external stress.[11] This study found that 50% of follicles with SSE showed inflammation. Kotrashetti *et al*. reported that 38.9% of follicles with SSE were associated with inflammation as compared to13.3% of cases with REE.[8] Simşek-Kaya *et al*. quoted study by De Paula *et al*. which suggested that chronic inflammation may cause chronic irritation and stimulate proliferation of epithelial cell.[9] A study by Yadav *et al*. noted a significant relationship between inflammation and presence of SSE.[3] Mesgarzadeh *et al*. found that 80% of inflammatory follicles showed pathological changes, while only 11% of noninflammatory dental follicles showed pathological changes.[16] This study found that incidence of the presence of SSE increases with age. In the age group of 25–29 years, 23.1% of follicles showed SSE whereas 38.5% of follicles showed SSE in the age group of 30 years and above. Khorasani and Samiezadeh found a significant relation between presence of squamous epithelium and age.[11] This study found odontogenic rest in 20% of cases. In Khorasani and Samiezadeh study, 48% of specimens showed odontogenic rests in CT.[11] Kotrashetti *et al*. reported the presence of odontogenic rests in 14.6% of follicles in their study. The presence of inactive odontogenic rests is frequent finding in follicles of normal developing tooth. Proliferation of odontogenic rests may indicate neoplastic change. Kotrashetti *et al*. quoted study by Lukinma *et al*. which suggested that the frequency and number of odontogenic epithelial rest appear to decrease with increase in the age of patients[8] [Table 4].

Conclusion

Within the limit of study population and method, we found slightly higher incidence of cystic changes in the age group of 18–24 years indicating the advantage of early removal, thereby

Table 4: Correlation of Histopathological parameters with age

Histopathological parameters	Age in years			*P*
	18-24 yrs (*n*=24)	25-29 yrs (*n*=13)	30 & above (*n*=13)	
Epithelium				
Absent	0 (0%)	3 (23.1%)	2 (15.4%)	0.047*
Present	24 (100%)	10 (76.9%)	11 (84.6%)	
type of epithelium				
REE	18 (75%)	7 (53.8%)	6 (46.2%)	0.477
SSE	6 (25%)	3 (23.1%)	5 (38.5%)	
Type of CT				
Loose fibrous	14 (58.3%)	8 (61.5%)	5 (38.5%)	0.127
Dense fibrous	10 (41.7%)	5 (38.5%)	8 (61.5%)	
Inflammation				
Absent	10 (41.7%)	2 (15.4%)	4 (30.8%)	0.058+
Present	14 (58.3%)	11 (84.6%)	9 (69.2%)	
Odontogenic rest				
Absent	18 (75%)	11 (84.6%)	11 (84.6%)	0.731
Present	6 (25%)	2 (15.4%)	2 (15.4%)	

reducing the surgical morbidity with increasing age. Vertically impacted position A LTM and pericoronal radiolucency in the range of 2.1–2.4 mm showed higher possibility of cystic changes. Our findings showed 24% cystic changes in normal radiographic pericoronal tissue. However, further clinical studies are required on large sample size to confirm these findings.

It is suggested for clinical and radiographic follow-up of impacted third molars. It is also recommended that histopathological analysis of the follicle should be conducted on all surgically extracted ILTM.

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Conflicts of interest

There are no conflicts of interest.

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