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RESEARCH ARTICLE

Cause and Effect Relationship Between Mandibular Third Molar Impactions and Associated Pathologies

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Abstract

Purpose: To determine and evaluate the possible causes for the development of pathological conditions associated with impacted mandibular third molars.

Methods: Sample comprised of 2292 impacted mandibular third molars reported to the Oral Diagnostics and Oral and Maxillofacial Surgery unit from December 2012 to June 2014. Radiographs were analysed for the presence along with type of impactions and associated radiolucencies. Excised lesions underwent histopathological examination. Chief complaints were recorded as pain, swelling, trismus and sensitivity in area of impaction.
Results: Male to female ratio was 1:1.7 with leading age range of 25-34 years. Prime chief complaint was pain (65.4%) with mesioangular (54.7%) as commonest type of impaction. Foremost associated pathology was pericoronitis (70.9%) followed by cysts (16.7%), facial space infection (9.9%) and tumors (2.2%) respectively. Maximum cysts (n=267) were associated with mesioangular impactions with periapical cyst in mainstream (87.9%). Majority of tumors (33.9%) were related to mesioangular impactions among which squamous cell carcinoma was maximum (n=12).
Conclusion: The early recognition of causes and monitoring of mandibular third molar impactions is imperative from a therapeutic point of view. To avoid prospective development of pathologies, we recommend regular screening of these teeth for appropriate clinical assessment and treatment planning.

INTRODUCTION

Abbreviations: IMTMs = Impacted mandibular third molars; SCC = Squamous cell carcinoma, KCOT = Keratocystic odontogenic tumor

Introduction

Tooth eruption is a normal physiological phenomenon that involves the movement of a tooth from its development site within alveolar process towards its natural functional position in the oral cavity [(1)]. However, several local or systemic factors can lead to failure of eruption of a tooth in its normal anatomic location. Therefore any tooth which is completely or partially unerupted and is positioned against another tooth, bone or soft tissue in a way that its further eruption is unlikely, as described according to its anatomic position, is known as impaction [(2,3,4,5)]. Impaction can be partial in case where the tooth is not completely encased in bone and is exposed in oral environment. Conversely, completely impacted tooth is one which is completely encased in bone and does not communicate with oral cavity [(2,6)]. Deciduous teeth impactions are extremely rare, but when occurs, it is mostly seen in second molars [(2)]. Among permanent dentition, mandibular third molars are most commonly impacted teeth accounting for over 80% of all impacted teeth [(3,7,8)]. These are followed by maxillary cuspids, maxillary third molars and mandibular second premolars respectively. However, impactions of incisors and multiple impactions have also been reported in the literature [(9,10)].

Many researchers have enlisted numerous local and systemic factors which may participate in the hindrance to tooth eruption. Systemic factors which can influence the impaction of permanent teeth include cleidocranial dysplasia, endocrine deficiency, febrile disease, Down syndrome, Gardner's syndrome, Gorlin-Sedano syndrome, Yunis Varon syndrome and irradiation [(10,11)]. Among local factors, prolonged deciduous teeth retention or early loss, malposed tooth germs, arch length deficiency, supernumerary teeth, trauma, odontogenic tumors, abnormal eruption path and cleft lip and palate may influence impaction of permanent teeth [(2,3,7,9,10,11)].

Despite of much advancement in the field of dentistry and unavailability of inadequate statistics regarding prevalence of pathologies in association with IMTMs, prophylactic removal of asymptomatic impacted third molars is still a debatable subject matter. Several researchers deem the notion that a strong indication of removal of IMTMs should be complemented by a strong contraindication for its retention [(12)].

In 1979, a Consensus Development Conference on removal of third molars was held at NIH (National Institute of Health) in order to formulate criteria for removal of impacted third molars. Issues explored as mentioned in the conference statement are;[(12,13,14)]

i) the effect of third molar removal on growth and development

ii) the timing and technical considerations for third molar removal

iii) prosthodontic and periodontic considerations for third molar removal

iv) the morbidity of third molar removal; and

v) the advantages and disadvantages of third molar removal

The conference participants devised a number of well-defined criteria for removal of third molars. Indications for removal as summarized are, in part, infection, nonrestorable carious lesions, cysts, tumors and destruction of adjacent teeth and bone. Less morbidity is associated with removal of these teeth in younger than in older patient. It was also suggested that morbidity and serious complications may be reduced if impacted teeth are removed at an early age.

Pericoronitis has been reported as the most frequently encountered pathologic condition and a well established indication for removal in association with IMTMs [6,7,12,15,16]. It is identified as an infection of the soft tissue that partially or totally surrounds the tooth[12]. Tissue coverage around impacted third molars may serve as an effective barrier to bacterial invasion[10,18]. Therefore status of eruption of mandibular third molar has significant implications in the development of pericoronitis around IMTMs[6]. Leone et al. enlisted risk factors for acute pericoronitis comprising of vertically positioned fully erupted mandibular third molar teeth which are in contact with second molar, above or along the occlusal plane having partial encapsulation of soft or hard tissues[12]. These parameters advocate IMTMs as premier teeth for prophylactic removal.

Development of cysts and tumors around IMTMs also entail these teeth as highest priority entrants for prophylactic removal. An incidence of 6.2% of cyst and tumor development has been reported in the literature [12,18]. Presence of long standing impactions is a strong risk factor for the progression of these pathoses. Consequently age of the patient has been marked as a strong predictor of cysts and tumors development around IMTMs. Patients falling in oldest age group (mean age 46.5 years) and youngest age group (mean age 20 years) categories are significantly prone to have these pathologic entities [8,12,18]. Highest probability of cystic changes is seen in unerupted mandibular third molars with bone and mucosa coverage[8,15]. Moreover, distoangular and vertical impactions have been revealed to have a close association with cyst development[8,19,20]. Numerous studies established measurement of pericoronal radiolucency representing follicular space around crown of impacted mandibular 3rd molar as an important criterion to assess cystic changes. It is documented that follicular space width of 2.5mm or larger is suggestive of cystic transformation around IMTMs[1,4,7,8,14,21,22,23]. Histopathologically, squamous metaplasia of pricoronal tissue can lead to cystic changes in dental follicle (3). Most commonly reported cysts in association with IMTMs are dentigerous cyst[1,8,21,24,25] and odontogenic keratocyst[19,21,24,26].

Among tumors, ameloblastoma is a frequent pathologic finding in relation to IMTMs[12,14,21]. Incidence of ameloblastomatous alterations has been reported to range from 0.14 to 2% among researchers[18]. Generally it is believed that ameloblastoma associated with follicular cysts developing around IMTMs decrease in prevalence after the age of 30 years due to transition of enamel organ epithelium to squamous epithelium [14].

Incidence of malignant tumors around IMTMs is very low. Few cases are reported about development of squamous cell carcinoma, odontogenic myxoma, odontogenic fibroma, fibrosarcoma and central mucoepidermoid carcinoma in association with IMTMs [12,27].

Another serious sequelae of mandibular third molar impactions is development of carious lesion on distal surface of adjacent second molars. Prevalence of second molar caries due to adjacent impacted third molar is approximately 3% [7]. However impacted third molars can also get carious attack themselves[4,10]. Numerous researchers designated caries as the most common pathologic condition associated with IMTMs. This finding disproves those who assert pericoronitis as the most frequently found pathology associated with IMTMs[4]. It is established that risk of

development of second molar caries is high in mesioangular and horizontal impactions[7,23]. This finding is attributed to the fact that third molar impactions having aforementioned angulations are partially exposed in the oral cavity leading to plaque accumulative crevices against distal surfaces of second molars, thus making these areas difficult to approach for tooth brushing, ultimately progressing to the formation of caries [10].

In many instances mandibular third molar impactions are asymptomatic unless some inciting factor leads to the emergence of symptoms. Therefore, Chu et al., reported only 30% of patients with mandibular third molar impactions presenting with symptoms[5]. Most common presenting complaints associated with IMTMs as presented in literature are swelling, pain, fever due to pericoronitis and loss of function[10]. Pain of varying degrees is a frequent concern for which patient seeks dental assistance[5,10,15]. Pain in otherwise asymptomatic IMTMs usually results from infection in the surrounding tissues. Another cause of pain could be the pressure on inferior alveolar nerve in deeply positioned mandibular third molar impactions [10]. According to many statistics accumulated worldwide, pain and swelling is more frequently associated with pericoronitis while some authors report these symptoms to be more commonly associated with cysts and tumors [5,7,12]. Moreover, Obeichiena et al. established that distoangular impactions have a noteworthy association with the development of pain [15].

The focus of present study is to scrutinize the pathologic sequelae of IMTMs and to set up the potential causes which lead to the development of most frequently encountered pathologies in our settings.

Materials and Methods

The sample for the present study was comprised of 1908 patients with 2292 IMTMs referred to the department of Oral Diagnostics and Oral & Maxillofacial Surgery, University College of Dentistry, University of Lahore, from December 2012 to June 2014. The protocols and guidelines for this study were approved by the Institutional Ethical Committee. The panoramic radiographs of 1908 patients were taken with original apparatus with a 1.27 magnification (Kodak 8000/8000C) following radiation protection protocol. Informed consent was taken from patients regarding purpose of research and assurance was given for strict confidentiality.

Radiographs were analyzed for the presence of IMTMs, type of impactions and associated radiolucencies. The radiographs were viewed on a radiographic view box by two experienced surgeons. One of them viewed 1450 radiographs and the other viewed 842 radiographs of IMTMs. To check the diagnostic reliability of the two examiners, 50 radiographs with radiographic lesions were examined in random order daily for five days assigned by them. The tooth was considered to be *impacted* if it failed to erupt completely in the oral cavity having partial or full coverage by bone or mucosa. When more than one lesion was found associated with a single IMTMs, then each lesion was recorded individually. Lesions were removed surgically along with involved IMTMs and examined histopathologically by two oral pathologists to minimize the inter-observer bias. The lesions were subsequently categorized as pericoronitis, cysts and tumors.

Inclusion criteria:

- Patients with age range of 20-50years

- Unerupted/ impacted/ partially erupted mandibular third molars
- Patients presenting with clinical symptoms which appeared due to mandibular third molar impactions

Exclusion criteria:

- Patients with greater than 50 years of age
- Fully erupted mandibular third molars
- Patients with congenital diseases or syndromes e.g. Down's syndrome and cleidocranial dysostosis
- Patients with a history of trauma or fracture that might have affected the normal growth of jaw affecting normal eruption of mandibular third molar
- Asymptomatic patients with IMTMs

Angulation criteria to assign type of impaction for IMTMs

Figure 1 illustrates the method to determine angular position of IMTMs. Two lines, each drawn individually along long axis of both impacted third molar and adjacent second molar were used to determine whether the impaction was vertical, mesioangular, distoangular or horizontal.

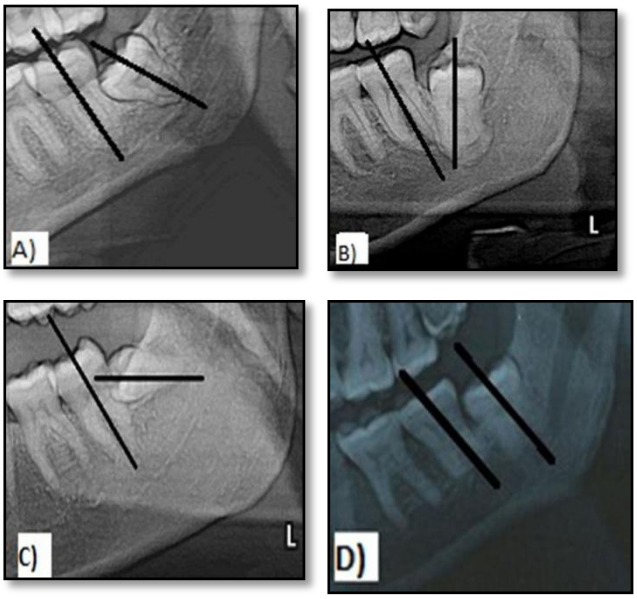

Figure 1: Diagrammatic representation of determination of angular position of impacted third molars A) Mesioangular impaction B) Distoangular impaction C) Horizontal impaction D) Vertical impaction

Criteria for diagnosing pericoronitis

Acute presentation was recorded. Acute and severe pericoronitis was identified as painful condition with fever, redness, swelling and/or purulence associated with IMTMs.

Criteria for diagnosing cystic lesion

Radiographically, follicular space equal to or greater than 2.5mm was suspected as cystic lesion around IMTMs. In panoramic radiographs, widest region of pericoronal space was measured by tracing both the contours of tooth and pericoronal space on a tracing paper. Two perpendicular lines, A-A and B-B, were drawn on the trace of tooth. Line A-A was drawn passing through the long axis of tooth and line B-B was drawn passing through centre of crown. From

the juncture point of two lines, a ruler (C-C) was moved to the widest point of the pericoronal space, where the measurement was carried out by vernier calliper (Fig 2).

Cystic lesions were further categorized into separate entities after histopathological examination. Cyst was nominated as *dentigerous cyst* when it showed the presence of cyst lining comprising of 4-6 layers of non keratinizing stratified squamous epithelium surrounded by dense, fibrous connective tissue wall. *Periapical cyst* was diagnosed when excised lesion showed lining of stratified squamous epithelium with acute and chronic inflammatory infiltrate.

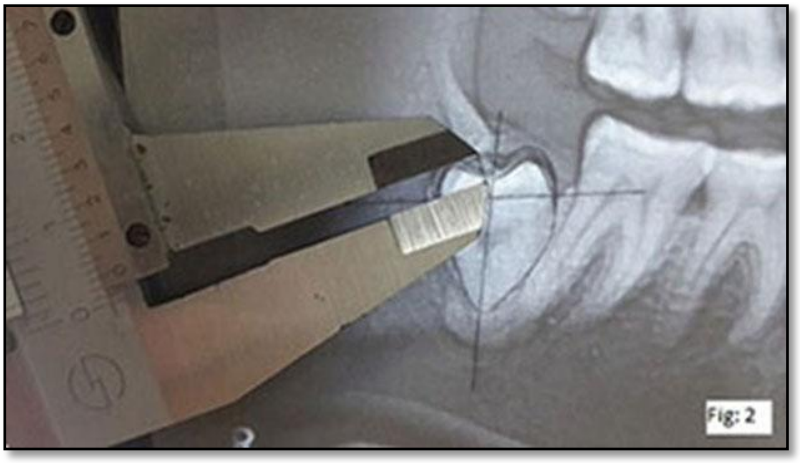

Figure 2: Method of measurement of follicular space by tracing panoramic radiographic image of IMTM on tracing paper

Criteria for diagnosing tumors

After clinical and radiographical evaluation and required investigations (CT Scan and MRI), biopsy was performed. Definite diagnosis was made after histopathological examination. *Ameloblastoma* was identified as either unicystic or polycystic, containing ameloblastic tumor cells, stellate reticulum and fibrous connective tissue. *Squamous cell carcinoma* (SCC) was diagnosed when features of anaplasia were seen in lining epithelium along with nests of atypical squamoid cells having keratin pearl formation. *Keratocystic odontogenic tumor (KCOT)* was included diagnosed when cyst lining was found to have 2-8 cell layer thick lining of parakeratinized stratified squamous epithelium.

Criteria for diagnosing facial space infection

A positive finding was considered when patient presented with swelling containing IMTMs with mesioangular and vertical angulations having carious lesions themselves, along with the presence of periapical radiolucency on radiographic examination.

Presenting complaint

Patient's chief complaints were grouped under four categories; pain, swelling, trismus and sensitivity in area of impaction.

Data was gathered and analysed using SPSS statistical package (version 20 software). Descriptive statistics were used to determine the frequency of variables. The relationship between type of impaction and associated pathology, cysts and tumors was analysed using Chi-square test. The level of significance was set at 5% ($p<0.05$).

Results

Among a total of 1908 patients included in the study period, 2292 impactions were recorded. Females (n=1215, 63%) outnumbered male patients (n=693, 37%) with a male to female ratio of 1:1.7. Most common age range was 25-34 years including 75% (n=1433) of patients followed by 35 – 44 years age group with 363 (19%) of patients.

Majority of the patients with IMTMs presented with the chief complaint of pain (n=1501, 65.4%) followed by 386 patients presenting with the complaint of limited mouth opening (16.8%) (Fig 3).Almost equal proportion of patients reported with sensitivity in adjacent second molar tooth (n=206, 8.9%) and swelling in the area of IMTMs (n=199, 8.6%).

Data regarding type of impaction revealed that most commonly found angulation of IMTMs was mesioangular (n=1255, 54,7%) followed by distoangular impactions which accounted 30% (n=688) of all the cases. The least frequent finding was vertical impactions consisting of 148 (6.4%) of the total sample (p=0.000). (Fig: 4)

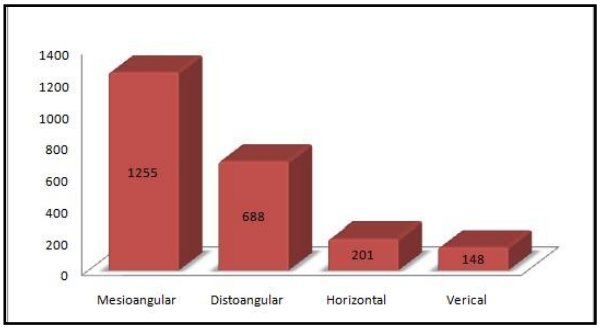

Figure 3: Distribution of type of impaction among patients with IMTMs (n=2292)

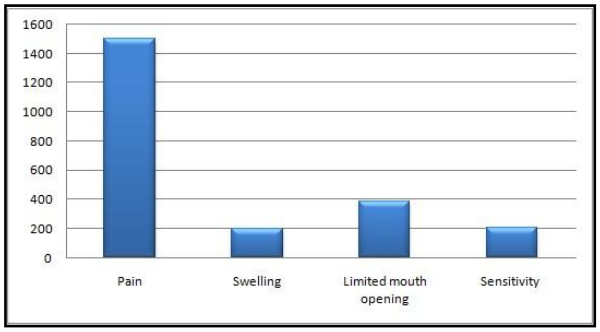

Figure 4: Distribution of chief presenting complaint among patients with IMTMs (n=2292)

Pathoses associated with type of impaction

The major pathologic conditions which were found in association with IMTMs were pericoronitis, cysts, tumors and facial space infection. If more than one pathology was found to be associated with single IMTM, then each lesion was recorded individually. A sum of 2371 aforementioned pathologic conditions was recorded in relation to 2292 IMTMs (p=0.000). Maximum number of lesions was recorded in association with mesioangular IMTMs (n=1274, 53.7%) followed by involvement of distoangular impactions including 704 (29.6%) pathologies. A count of 236 (9%) pathologic conditions was made in association with horizontal IMTMs while vertical impactions least commonly contained lesions with a total number of 157 (6.6%) pathologies.

Most frequent pathologic condition that was encountered in association with IMTMs was pericoronitis with a sum of 1685 (70.9%) cases. This was followed by cysts (n=398, 16.7%), facial space infection (n=235, 9.9%) and tumors (n=53, 2.2%) respectively. (Fig: 5)

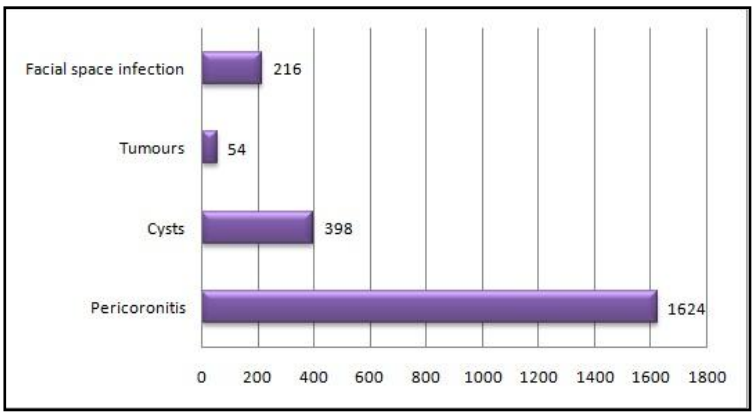

Figure 5: Relative frequency of pathologies associated with IMTMs (n=2292)

Among 1274 lesions found in association with mesioangular impactions, maximum number was occupied by pericoronitis with 883 (69.3%) cases followed by cysts with 267 (20.9%) cases. Next in the count were 106 (8.3%) cases of facial space infection associated with mesioangular impactions. A total of 591 (83.9%) cases of pericoronitis were found in relation to mesioangular impactions followed by facial space infection which comprised of 78 (11%) cases. Among 236 lesions which were associated were horizontal impactions, largest proportion (n=114, 48.3%) comprised of pericoronitis followed by cysts with 86 (36.4%) cases. A count of 97 (61.7%) cases of pericoronitis was recorded in association with vertical IMTMs. Cases of cysts and facial space infection in relation with vertical impactions held almost equal proportion with a count of 26 (16.5%) and 25 (15.9%) respectively. (Table: 1)

Type of impaction	Pericoronotis	Cysts	Tumours	Facial space infection	Total
Mesioangular	883	267	18	106	1274
Distoangular	591	19	16	78	704
Horizontal	114	86	10	26	236
Vertical	97	26	9	25	157
Total	1624	398	54	216	2371

Table 1: Distribution of pathologies associated with different types of IMTMs

Cysts and type of impactions

Among cystic lesions, periapical cyst (n=350, 98.1%) and dentigerous cyst (n=48, 12%) was diagnosed in association with IMTMs (p=0.000). Maximum number of cystic lesions (n=267,67%) were found to be associated with mesioangular impactions (Table:1) out of which periapical cyst with 262 (98.1%) cases outnumbered dentigerous cyst with a count of 5 (1.8%) cases. (Table: 2)

These results were followed by horizontal IMTMs which accounted for 86 (21.6%) cases of cysts (Table:1) among which periapical cysts were 70 (81.3%) in number while 16 (18.6%) cases consisted of dentigerous cyst. (Table: 2)

Next in the count was vertical IMTMs with 26 (6.5%) cysts (Table:1) with maximum number revealed to be dentigerous cysts (n=21, 80.7%) followed by periapical cysts (n=5, 19.2%). (Table: 2)

The least number of cystic lesions was found in relation to distoangular impactions with 19 (4.7%) cases (Table:1) out of which majority was occupied by periapical cyst with 13 cases (68.4%) as compared to 6 (31.5%) cases of dentigerous cyst. (Table: 2)

Type of impaction	Periapical cyst	Dentigerous cyst	Total
Mesioangular	262	5	267
Distoangular	13	6	19
Horizontal	70	16	86
Vertical	5	21	26
Total	350	48	398

Table 2: Frequency of periapical cyst and dentigerous cyst among different type of impactions

Tumors and type of impaction

Out of total 53 cases of tumors (p=0.003), maximum number of lesions (n=28, 52.8%) were diagnosed as KCOT followed by SCC with a count of 21 (39.6%) cases. Only 4 (7.5%) cases were diagnosed as ameloblastoma. (Table: 3)

Maximum number of tumors (n=18, 33.9%) was found to be associated with mesioangular IMTMs among which SCC turned out to be most frequent lesion (n=12, 66.6%) followed by KCOT with 6 (33.3%) cases. No case of ameloblastoma was found in relation with mesioangular impactions. (Table: 3)

This finding was followed by distoangular IMTMs with 16 (30.1%) cases of tumors showing equal results for SCC and KCOT, each having 8 (50%) cases. Finding related to ameloblastoma were similar to that of mesioangular IMTMs with no diagnosed case related to this type of impaction. (Table: 3)

Next in the count were horizontal IMTMs with 10 (18.8%) cases of associated tumors. In this category, KCOT outnumbered the rest of two entities with 7 (70%) cases. This was followed by ameloblastoma (n=2, 20%) and SCC (n=1, 10%) respectively. (Table: 3)

Among vertical IMTMs, 9 (16.9%) cases of tumors were detected out which none was diagnosed as SCC. Maximum number of cases were diagnosed as KCOT with 7 (77.7%) cases. Likewise horizontal IMTMs, vertical impactions also held 2 (22.2%) cases of ameloblastoma. (Table: 3)

Type of impaction	SCC	KCOT	Ameloblastoma	Total
Mesioangular	12	6	0	18
Distoangular	8	8	0	16
Horizontal	1	7	2	10
Vertical	0	1	2	9
Total	21	28	4	53

Table 3: Frequency of SCC, KCOT and Ameloblastoma among different type of impactions

Discussion

Mandibular third molar impaction has become a frequent dental discovery over a period of last few decades affecting that proportion of population which engages the normal eruption age range of third molars. This finding remains unveiled until patient undergoes radiographic investigations for supplementary dental ailment or when any symptom/complication associated with third molar impactions becomes apparent. Numerous studies across the globe report progression to pathological changes in long standing impactions. Apart from mainstream pathologies associated with IMTMs e.g. pericoronitis, second molar caries, cysts and tumors, unusual lesions like actinomycosis and foreign body granuloma have also been reported in the literature [4,8,12,23,27]. These judgments favor prophylactic removal of IMTMs by many surgeons in order to avoid higher cost of extraction if performed after pathology has developed as well as morbidity associated with the quick rate of succession of untreated pathological conditions.

This study was performed in an attempt to evaluate possible causes of development of pathoses as a sequelae of IMTMs, although not all IMTMs cause clinical problems and the percentage of IMTMs that may remain asymptomatic for years is unknown [22]. In current investigation, 75% (n=1433) of the patients reported with symptomatic IMTMs occupied age range of 25-34 years. These findings were in accordance to several well reported studies in literature [5,7,12]. On the other hand **Al-Khateeb and Bataineh** [4] and **Shetty et al.,** [28] showed peak prevalence of 20-25 years of age among patients with IMTMs and associated pathologies. These variations in the age distribution may be attributed to the wide range of normal eruption timings of mandibular third molars as well as to the differences in the social and cultural norms in various geographic regions athwart the globe.

Moreover, a gender-wise division analysis of histopathological diagnosis of pathoses associated with IMTMs revealed a female predominance over male patients with a male and female ratio of 1:1.7. These results were similar to those depicted by many researchers[5,12,15,23] while many others discovered males involved in majority[4,7,10]. The reason for this gender dissimilarity is not clear. A possible explanation could be the anatomical differences in jaw size among males and females as well as the racial diversity all the way through the world.

In present study, outcome of data regarding chief presenting complaint revealed maximum patients presented with pain (n=1501, 65.4%) in the area of mandibular third molar. This finding was in line with various studies worldwide[5,10,12,14,15 20]. This result was followed by 16.8% (n=386) cases presenting with complaint of limited mouth opening. This entity was also mentioned by **Keskin and Akal** as one of the multiple presenting complaints in their study[12]. However, Stanley et al as well as **Adeyemo and Msagati et al.,** cited *'trismus'* as postoperative complication following surgical removal of impacted third molars rather than as presenting complaint [10,14,18]. In current study, next in the count of chief presenting complaint was sensitivity in adjacent second molar teeth (n=206, 8.9%) due to carious lesion formed as a result of surface approximation of IMTMs. Second molar caries were taken into account by several researchers as most commonly found pathologic condition associated with IMTMs [4,23]. However, in this study, sensitivity of second molar tooth due to presence of carious lesion was considered more appropriate to be taken as presenting complaint. Lastly, 8.6% (n=199) cases presented with the chief complaint of swelling. This finding

conforms well to the data found in literature [12,14] except few studies which pointed out swelling as postoperative complication following surgical removal of IMTMs [10,14].

In current study, mesioangular IMTMs were in majority with 54.7% (n=1255) of cases followed by distoangular (n=688, 30%) and horizontal (n=201, 8.7%) impactions respectively. Vertical impactions were found least in number with 6.4% (n=148) of cases. The results for mesioangular IMTMs were similar to those mentioned by many other researchers [7,10,12,23]. On the other hand, **Stanley et al.,** in their study reported vertically IMTMs existing in majority followed by mesioangular impactions [14].

In this study, pathologies were mostly found in association with mesioangular IMTMs with 53.7% (n=1274) of cases followed by distoangular (n=704, 29.6%), horizontal (n=236, 9%) and vertical (n=157, 6.6%) impactions respectively. Results for this particular characteristic vary among various studies conducted worldwide. **Polat et al.,** demonstrated mesioangular and horizontal impactions to be most commonly associated with pathoses in relation to IMTMs[23]. Likewise **Simsek-Kaya et al**., depicted mesioangular along with distoangular IMTMs to bear greater chances of development of pathologies [22]. On the contrary, Knutsson et al showed distoangular as the type of IMTMs to become more associated with pathologies[12]. This inconsistency in evidences may be attributed to ethnic, regional and social diversity among different regions of world.

In present study, the most frequently diagnosed pathology associated with IMTMs was pericoronitis comprising 70.9% (n=1685) of all lesions. These findings were analogous to those mentioned by **Obiechina et al.,**[15] and **Patil**[7] in their evaluation of symptomatic conditions associated with IMTMs but were contradictory to those presented by **Al-Khateeb et al.,** and **Polat et al.,** [4,23] who established carious lesions of second molar teeth adjacent to IMTMs to be the most commonly found lesion.

In current investigation, maximum number of cases of pericoronitis (n=883, 69.3%) were found in relation to mesioangular IMTMs. This evidence was in accordance to that depicted by **Knutsson et al.,**[12] but contrary to that which was provided by **Shira** [16] and **Indira et al.,**[6] who established that mostly vertical and distoangular IMTMs lead to development of pericoronitis. One possible explanation of disparity in these findings is that level of eruption of mandibular third molar and overlying soft tissue coverage could be more dependable predictors of development of pericoronitis as compared to angulation of IMTMs. Another probable reason as mentioned by **Shira**[16] was the establishment of a positive correlation between the distance from the midpoint of ramus to the midline of arch and development of acute pericoronitis; greater the distance, the greater the chance of disease. This owes to the continuous growth of mandible assisting the entrance of third molar crown in oral cavity which is mandatory for the disease to occur.

Cysts encompass second most common pathological condition with 17.3% (n=398) in current study. Findings in this study suggest maximum number of pathologies (n=267, 89.5%) diagnosed as a cyst was associated with mesioangular

impactions. A wide divergence was seen in results showed by **Knutsson et al.,** and **Adaki et al**. The former showed horizontal IMTMs to be more associated with cystic changes while latter established development of cystic lesions in association with distoangular impactions[8,12]. Like many other researchers, measure of >2.5mm of follicular space on orthopentamorgam (OPG) was considered evocative of cystic change in present study [8,22,23]. In contrast **Mesgarzadeh et al.,** and **GUNDUZ et al.,** suggested >3mm and >4mm of follicular space respectively around impacted third molar as well as non-third molar impactions as reliable indicator of presence of cysts [3,27]. Cystic changes in follicular tissue can also be determined by MCM2, Ki-67 and PCNA immunohistochemistry [8,22].

Along with many others, **Patil** and **Mesgarzadeh et al.,** demonstrated dentigerous cyst as the most prevalent cystic lesion in association with IMTMs[7,27]. This verdict was in contradiction to that of current investigation where lesions diagnosed as periapical cyst (n=350, 87.9%) outnumbered those diagnosed as dentigerous cyst (n=48, 12%). During literature search, very few studies were found regarding periapical cyst development in relation to IMTMs. However **Al-Khateeb et al.,** studied radiolucencies around IMTMs under two categories, pericoronal radiolucencies and periapical radiolucencies. The former were found to be the cysts and tumors with dentigerous cyst forming the majority. The latter were diagnosed as chronic periapical inflammation either in the form of periapical granuloma or periapical cyst[4]. These results were computed as caries of third molar themselves were taken into account in the aforementioned study, a feature which is not frequently recorded leading to paucity of available reported data regarding periapical cyst. In present study, sequelae of carious lesion of third molar were given serious consideration and taken as study parameter instead of carious lesions themselves. One of the possible reasons for periapical cysts being the mostly encountered cystic lesion in current analysis could be the unawareness of presence of impaction and lack of oral hygiene habits in general population in this region. Even among the patients who practice adequate oral hygiene modalities can develop caries in third molars due to difficult approach of third molar containing area in oral cavity thus making another probable cause of acquisition of periapical cyst[10]. Another possible factor contributing in third molar caries could be the overlying bone and soft tissue coverage. Partially erupted third molars are more prone to carious attack and subsequent periapical lesion formation than unerupted and IMTMs.

An atypical pathological finding in the current study was development of facial space infection in association with IMTMs. A count of 216 cases (9.4%), less in number than cysts and greater in number than tumors in association with IMTMs, was revealed in this investigation. A deep insight in literature regarding incidence and development of deep abscess formation related to IMTMs is quite sparse. However, **Patil** in his study mentioned this pathology as a rare judgment related to impacted third molars [7]. Moreover, **Stanley et al.,** and **Duarte et al.,** brought up this entity as postoperative complication following surgical removal of IMTMs along with associated pathology[9,14]. In present investigation, maximum number of cases of facial space infection (n=106, 49%) were found developing along mesioangular IMTMs. Association of facial space infection with third molar impaction is still a debatable subject matter which requires more exploration and investigation to institute obvious facts and figures. Only study that was found during literature search elucidated no significant impact of type of impaction in predicting development of facial space infection [26].

According to recent World Health Organization's specifications, odontogenic keratocyst in present study was taken under the category of tumors with the revised nomenclature of keratocystic odontogenic tumor (KCOT) making up majority (n=28, 52.8%) of diagnosed cases of tumors in association with IMTMs. Second in the order was squamous cell carcinoma (SCC) (n=21, 39.6%) and ameloblastoma (n=4, 7.5%) respectively. These results were in entire contradiction to world's reported data where ameloblastoma was established as the most frequently developed tumor in association with IMTMs[4,7,27]. However, considering KCOT as odontogenic keratocyst, **Rakprasitkul** in his study depicted it as more frequent pathologic change as compared to ameloblastoma[21]. Furthermore, numerous case reports showing KCOT in relation to impacted third molars are found in literature [19,24,26] but wide scale analysis of this finding is scarcely found in studies. Similarly, development of SCC as discovered in present study is also a little reported entity in literature. Though **Guven et al.,** mentioned a single case of SCC diagnosed in association with IMTMs [12].

Results of current investigations show that impaction of mandibular third molar teeth is a commonly discovered dental anomaly that usually remains unnoticed by the patients unless some symptoms ensue. The early recognition of pathological conditions associated with IMTMs along with potential causes is especially important from a therapeutic point of view. As showed in present study, impacted teeth may result in many serious complications like cysts, pathological fractures and tumors, thus making early detection imperative to circumvent loss of several anatomical vital structures present in close proximity of these teeth. It is concluded that patients falling in the age range of 25-34 years, presenting mostly with pain and having mesioangular type of impactions are at greater risk of developing associated pathologies, therefore must be considered as priority candidates for removal of IMTMs.

The results in this study were similar to the data reported in the literature with few exclusive discoveries. Other dissimilarities may be attributed to limits of population as well as materials and methods. In order to avoid prospective development of pathological conditions in association with IMTMs, we recommend monitoring of these teeth whether or not they are symptomatic. Furthermore, we commend histopathological analysis of all surgically removed tissue along with IMTMs to cater the need of appropriate assessment and later on follow- ups.

Conflict of Interest: None

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Wajiha Alamgir made the literature research, reviewed the cases and made the whole writing. Muhammad Mumtaz worked on clinical data and statistical analysis of the results. Farhat Kazmi contributed with histopathological review, classification of cases and compilation of results.

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