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ORIGINAL ARTICLE

ASSOCIATION BETWEEN ANGULATION OF MANDIBULAR THIRD MOLAR IMPACTIONS WITH FACIAL SKELETAL TYPES AND CEPHALOMETRIC LANDMARKS

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ABSTRACT

OBJECTIVES: To determine the association of impacted mandibular third molar with skeletal facial types and different anatomical and cephalometric landmarks.

METHODS: This cross-sectional study was conducted at Rehman College of Dentistry and Khyber College of Dentistry, Peshawar, Pakistan from October to December 2020. Panoramic and lateral cephalometric radiographs of 800 patients (aged 22-35 years) were retrieved from the records. Third molar impaction was classified by Winter's classification using IC Measure software. The skeletal facial type was determined by measuring Point A Nasion Point B angle using Viewbox software. An association of third molar impaction with skeletal facial types, cephalometric and anatomical variables was evaluated.

RESULTS: The most common mandibular tooth impactions type was Mesioangular impaction (81.3%) and skeletal facial type was skeletal class-I (47.5%). Comparative analysis among different impaction types using One-way ANOVA showed that although these impaction types did not differ significantly in terms of skeletal facies (p=0.07), significant difference in terms of age (p=0.028), Maxillary Mandibular Plane Angle (MMPA) (p=0.007), depth (p=0.000), ramus relation (p=0.000) and inferior dental nerve (ID) canal (p=0.001) were observed. ID canal was found to be positively but weakly correlated (r=0.2) with impaction types. Contrariwise, depth and ramus relation showed moderately negative correlation (r=-0.40 and r=-0.30, respectively) with impacted tooth angulations.

CONCLUSION: Although it is difficult to predict the impaction type in patient based on their skeletal facies, associations between other anatomical and cephalometric variables were observed which may help in predicting the degree of difficulty that may be encountered during the surgical procedures.

KEYWORDS: Tooth, Impacted (MeSH); Impaction (Non-MeSH); Molar, Third (MeSH); Cephalometry (MeSH); Cephalogram (Non-MeSH); Orthopantomogram (Non-MeSH); Inferior dental canal (Non-MeSH); Mandible (MeSH)

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INTRODUCTION

The impacted tooth is the one which has failed to fully erupt into the oral cavity within its expected developmental time period i.e. between the age of 17-21 years.[1] The most commonly impacted tooth is mandibular third molar.[2] The causes of impaction are both local and systemic such as lack of space, retained deciduous tooth, obstruction in path of eruption, pre and postnatal and syndromes.[3] The widely followed classifications of the impacted mandibular third molars are the Winter's (1926) and Pell & Gregory's (1933) classifications.[4,5] Winters has classified the impacted tooth into various categories (a, b, c, d, e) according to the angle formed between the long axis of the second and the third molar.[4] Pell and Gregory's classified third-molar impaction on its relationship with the ramus of the mandible (Class I, II and III) and position analogous to the occlusal plane (Class A, B and C).[5]

The most frequently encountered impaction is mesioangular and the most difficult tooth to extract is distoangular.[6] The presence of impacted third molar can lead to recurrent pericoronitis, dental caries in adjacent tooth, periodontal disease and root resorption of adjacent tooth.[7] Those impactions which become clinically symptomatic in recurrent fashion, they may have to be dealt surgically. The surgical removal of third molars can result in intra or postoperative complications such as alveolar osteitis (AO), infection, bleeding and paresthesia.[8]

In order to evaluate the position of the impacted tooth and prevent intra and postoperative complications, orthopantomogram (OPG) is advised. OPG evaluates the position and angulation of impacted third molar, its association with the Inferior Dental Nerve (IDN), depth of the impacted tooth and ramus relationship/ space available.[9] The four common treatment options for impaction are observation, intervention, relocation and extraction.[10] Many indices have been proposed for an appropriate treatment plan and to assess surgical difficulty so that none or minimum postoperative complications develop. Neither of them is universally applicable and has its limitations. They are generally based on the angle of impacted tooth, its depth, ramus relation, proximity to the inferior dental nerve (ID) canal, alveolar bone density, tooth morphology.[4,5] In general, the risk of complication in decreasing order according to impaction type is Distoangular (6.5%) followed by Mesioangular (4.5%), Horizontal (4.0%) and Vertical (2.7%).[7]

There are some cephalometric parameters and angles that can help predict the difficulty index of the impaction and are measured through lateral cephalogram. It is a radiograph widely used in orthodontics (cephalometric tracing), orthognathic treatment, and maxillofacial surgeries and to assess skeletal facial growth pattern.[11] The cephalometric angles measured in our study are Sella Nasion PointA (SNA), Sella Nasion Point B (SNB), Point A Nasion Point B (ANB) and Maxillary Mandibular Plane Angle (MMPA). According to the ANB angle (SNA-SNB) the skeletal facial types are classified into three (1): (a) Skeletal class I (ANB: 1-5 degrees), (b) Skeletal class II (ANB more than 5 degrees) and (c) Skeletal class III (ANB less than 1 degree).

Due to extensive variations not only among different populations but even within the population, there is limited data on the association of impaction with the skeletal facial growth. This study aims at determining the relationship between impacted third molar and facial skeletal type. Since the type of impaction has a bearing upon risk of complications, we by determining this association, may be able to predict the type of impaction which patient may develop and risk of complications more precisely during the surgical procedures.

METHODS

This cross sectional study was carried out at Rehman College of Dentistry (RCD) and Khyber College of Dentistry (KCD), Peshawar, Pakistan from October to December 2020. Sample size was calculated using open epi calculator. Since, RCD and KCD receives approximately 200 patients per month hence, over the period of six months, we expected the unit to receive 1200 patients. With 95% confidence level, anticipated population proportion of 0.80, 0.05 absolute precision, and relative precision of 0.0625, the calculated sample size was 798. Therefore, a total of 800 archived records (in soft form) of the patients between 22-35 years of age were taken. Those with fully impacted mandibular third molars and non-extracted adjacent teeth were included and those above or below the required age, with absent second mandibular molar and local pathologies were excluded. Their lateral cephalograms and OPGs were used for the readings (Figure 1). Patient information like demographics and clinical examination were recorded on a purposefully designed proforma. OPG was used to find the angulation and depth of the impacted mandibular third molar, its ramus relation and association with inferior alveolar canal. This was done by using a software IC Measure version 2.0.0.245. (Figure 1) The main landmarks of OPG were traced and then the following findings made:

A) The angle of the impacted molar was formed by the lines passing through the long axis of second and third mandibular molars from the midpoints of occlusal surface and root bifurcation.[12]

B) Depth was classified into A, B and C.[5] If the crown of impacted third molar was at the same level or above the highest portion of the crown of the second molar it was classified as A. If it was below the highest portion of the crown of the second molar and above its cervical line then it was level B and if the crown was below the cervical line of the second molar then it was considered as level C.[5]

C) Ramus relation determines the space available for the mandibular third molar to erupt.[5] It is defined as an eruption space between ascending ramus to the distal of second molar. An occlusal plane was first drawn by extending a line from the highest cusp tip of first premolar to the mesial cusp tip of second molar till the ascending ramus. A perpendicular line was drawn from occlusal plane at the distal of the second molar. The space between the distal of second molar and ramus was then measured. The width of crown of impacted tooth was also measured and ratio taken[12] (Figure 2). The ratio between the two was calculated to measure eruption space. If it was more than two-thirds it was considered as Class I, if it was between one-third and two-thirds it was Class II and if it was less than one-third it was classified as Class III.

D) The relation of the roots of the mandibular third molar with the border of inferior alveolar canal was assessed visually (Figure 2). The deflection, darkening and narrowing of the root or interruption of the white line of the canal or any narrowing and diversion of the canal and/or dark and bifid root apex were in close proximity to the ID canal.[13]

The cephalometric angles (SNA, SNB, ANB and MMPA) were measured by the cephalometric analysis using lateral cephalogram. Landmarks were identified and then linear and angular measurements were taken. This was done using a CE-certified software, View Box. The patient's facial skeletal type was classified from ANB.

The data was recorded and analyzed using SPSS version 20 and MS excel. The descriptive statistics were used to calculate Mean ± standard deviation for all numerical variables such as age and cephalometric measurements. While categorical variables such as facial skeletal types, third molar impaction types, ramus relation and inferior alveolar canal and depth of impacted tooth were presented in the form of frequencies and percentages. For quantitative variables, ANOVA followed by Post-Hock Tukey test was used while for categorical variables Chi-square test was used to compare the means of the groups. The association of cephalometric angles and anatomical landmarks with the type of impaction was determined using Spearmen correlation. (Figure 3)

RESULTS

Of the 800 patients, 366 (45.7%) were

male and 434 (54.3%) were female. Patients ranged in age from 22 years to 35 years with mean age of the study sample was 25.92±3.23 years. The mean age in skeletal class I was 26.09±3.11 years whereas in class II it was 25.5±3.32 years and in class III it was 25.9±3.33 years. The mean age of samples having horizontal, vertical and any other angulation was 24.8±3.01, 24.6±3.49 and 24.6±1.36 respectively whereas in mesial angulation it was 26.04±3.18 years while for distal angulation it was 26.05±3.55 years. In case of gender distribution, more females exhibited Class I (58.42%) and II (62.19%) facial skeletal type. Mesial, distal and any other had more females than males. Horizontal angulation on the other hand, had more male population.

the table in terms of its types, depth is presented as levels A, B and C while Ramus relation is shown in terms of its classes I, II and III (see methods). As can be seen from the table II, most subjects of impacted tooth angles, depth and ramus relation come under the normal facial height category. Furthermore, class III ramus relation is common in smaller facial height as compared to the normal and long face.

In case of depth of the impacted tooth, overall level A depth was observed in 446/800 (55.8%) samples. In ramus relation, Class I constituted about 574/800 (71.8%) of the samples whereas 48% of the impacted third molars had close proximity to the ID canal. The frequency of impacted depth. Interestingly, none of the distally impacted teeth and those having any other angulation were found at level C.

Approximately, 45% of the mesially impacted teeth had close proximity to inferior dental canal showing the highest percentage among all the categories. On the other hand, in comparison to all angulations, 75% of the distal impaction showed no proximity to the inferior dental canal. An important finding however, was that the teeth in any other category had 0% proximity to the inferior dental canal. A comparative analysis was done among different mandibular impaction types with variables using one-way ANOVA. It showed significant difference in terms of age, MMPA, depth, ramus relation and ID

TABLE I: MEAN AND STANDARD DEVIATION OF CEPHALOMETRIC LANDMARKS

Cephalometric angles	Mean ( )	Std. deviation	Minimum	Maximum
Sella Nasion Point A (SNA)	80.31	4.24	63.5	95.1
Sella Nasion Point B (SNB)	78.12	3.99	67.2	92.7
Point A Nasion Point B (ANB)	2.19	3.55	-14.4	11.8
Maxillary Mandibular Plane Angle (MMPA)	25.89	6.84	9	53

TABLE II: DESCRIPTIVE ANALYSIS OF MAXILLARY MANDIBULAR PLANE ANGLE WITH OTHER ANATOMICAL VARIABLES

MMPA	Tooth angles					Depth			Ramus relation		
	Mesial	Distal	Horizontal	Vertical	Any other	Level A	Level B	Level C	Class I	Class II	Class III
< 22ÿ	170	24	14	14	0	106	70	46	148	64	10
22-32ÿ	352	38	16	14	6	242	120	64	310	112	4
> 32ÿ	128	18	2	4	0	98	38	16	116	34	2

MMPA=Maxillary Mandibular Plane Angle

Mesioangular impaction (81.3%) was the most common amongst all type of the mandibular tooth impactions, while overall, Class I facial skeletal type was found to be 47.5% of all three types while class II and III were 20.5% and 32.0% respectively. A range of cephalometric landmarks were determined. Mean Sella Nasion Point A was 80.31±4.24° and Sella Nasion Point B was 78.12±3.99° (Table I).

Analysis of MMPA with the various tooth angles, depth of the impacted tooth and its ramus relation was done. MMPA is divided into three: <22° (short facial height), 22-32° (normal facial height) and >32° (long facial height). While the tooth angles are mentioned in mandibular tooth angulations in facial skeletal types was also measured. The skeletal class I had the highest proportion of vertical tooth angulation (62.5%). Skeletal class III on the other hand, comprised mostly of distal angulation (42.5%). There was however, an equal prevalence of any other tooth angulation in all three skeletal classes (33.3%).

The frequency of depth among different tooth angulations was also measured. Among all of the impacted molars, 75% of distally and vertically impacted teeth were at level A making the highest percentage of this class of depth. Horizontally impacted teeth however, had the maximum of level B (44%) and C (19%) canal, suggesting that the five impaction types differed significantly in terms of these parameters only. In order to test which impaction type differed significantly from others, we carried out Post Hoc analysis (Tukey test). With this analysis, it was evident that in terms of MMPA, only distal impaction was significantly different from horizontal type. Similarly, in terms of ramus relation, distal impaction was significantly different from mesial, horizontal and vertical impaction. In case of depth, mesial impaction was significantly different from distal and horizontal impactions. In ID canal, mesial was significantly different from horizontal impaction.

In order to determine the correlation

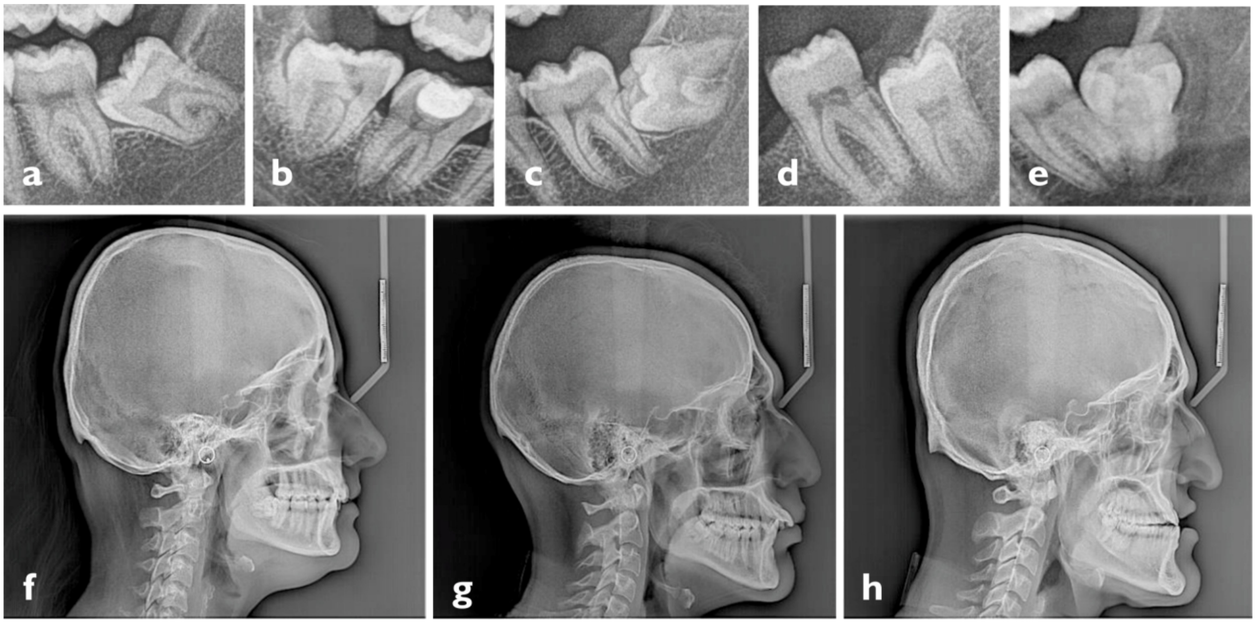

Figure 1: Cropped digital panoramic radiographic showing examples of Winter's classification. (a) mesioangular, (b) distoangular (c) horizontal (d) vertical (e) any other. Figure f-h showing facial skeletal types. (f) class I, (g) class II and (h) class III

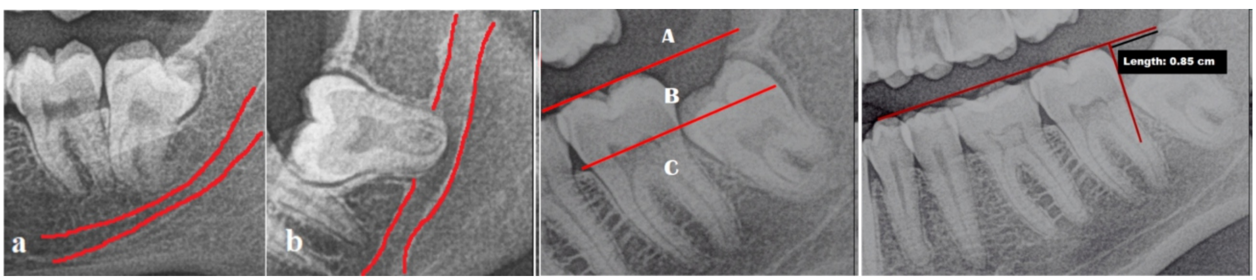

Figure 2: a and b showing the proximation of third mandibular molar with inferior dental canal. The red lines map the ID canal a) no proximity to the ID canal (b) close proximity to ID canal with interruption of ID canal (c) showing different depths (A, B and C) of the impacted tooth is measured (d) shows how the ramus relation is calculated.

between different categories of impactions (i.e. mesial, distal, horizontal, vertical and any other) and skeletal facies (i.e. Class I, II, III), Spearman correlation statistics were run. Interestingly, no correlation was found between impaction types and skeletal facial types (p=0.293, r=0.037). In case of association between tooth angles and ID canal (p=0.000) it was found to be significant however, they were positively but weakly correlated (r=0.20).The teeth angulations and ramus relation were significant (p=0.000) and negatively but moderately correlated (r=-0.3). The association between the teeth angles and the depth of the impacted tooth was also significant and moderately negatively correlated (p=0.000, r=0.4). The tooth angles and age had an association with a negative weak correlation (p=0.05, r=-0.07). The association between the skeletal facial types and the ramus relation was significant and weakly negatively correlated (p=0.04, r=-0.073). The ID canal was significantly associated with the depth of the tooth with a weak positive correlation (p=0.000, r=0.3). It also had a significant association with the ramus along with a weak positive correlation (p=0.014, r=0.1). The correlation of MMPA with the depth of the impacted tooth was weak and negative (p=0.002, r=-0.11) and with ramus relation was also significant and weakly negatively correlated (p=0.015, r=-0.086). Ramus relation was significantly associated with the depth of the impacted tooth and showed a moderate positive correlation (p=0.000, r=0.3). It also showed significance with age as well (p=0.000) but with a negative weak correlation (r=-0.138).

DISCUSSION

The aim of this study was to determine the association between the angulations of mandibular third molar impaction with the facial skeletal types as well as with different cephalometric and anatomical landmarks. This study was carried out on the archived records using OPG and lateral cephalogram. Interestingly, no association was observed between the tooth angle and facial skeletal types, still varied degrees of associations were found between other variables such as ramus relation and tooth angulations. These findings suggest that although it is difficult to predict the type of impaction in patients presenting with different skeletal facies, the associated cephalometric and anatomical landmarks are somewhat easily predictable. Thus these associations may be useful in predicting the extent of difficulty during the tooth extraction if required.

From our study it was observed that there were more females than males in most of the impacted tooth angulations whereas the study conducted by Gumrukcu[14] showed gender predisposition for females too. This may be attributed to female growth stopping the time the impacted tooth erupts whereas in males it does not hence the jaw keeps growing creating space for the tooth to erupt.[15] On the other hand, females also tend to be more aesthetically conscious hence report more to the hospital for impacted third molar removal.

In our study the most commonly impacted angulation type was mesial. We used Winter's classification for the impacted teeth. Two studies which have used the similar method of classification also found mesial to be the most common.[6,15] As far as association in terms of frequency is concerned the vertical impaction was found to be the highest in class I skeletal facial type (62.5%) as compared to the other two classes. However contrary findings were observed by Breik et al.[16] who found horizontal impaction to be highest in dolichofacial (another type of facial classification) subjects. The difference can be due to the different classification of skeletal facial types used for the analysis. They classified into brachy, mesio and dolichofacial according to facial axis angle in which a vertical facial growth pattern was observed whereas in our study horizontal growth pattern was observed. The great majority of the subjects in our study belong to skeletal facial type I (47.5%). Samare et al. in their study also reported skeletal facial type I to be more prevalent (37%).[17] This similarity may be attributed to it being carried out on Asian population. However in a study which was conducted on German population equal proportion of subjects were observed in all three skeletal facial types.[18]

The measurements of cephalometric

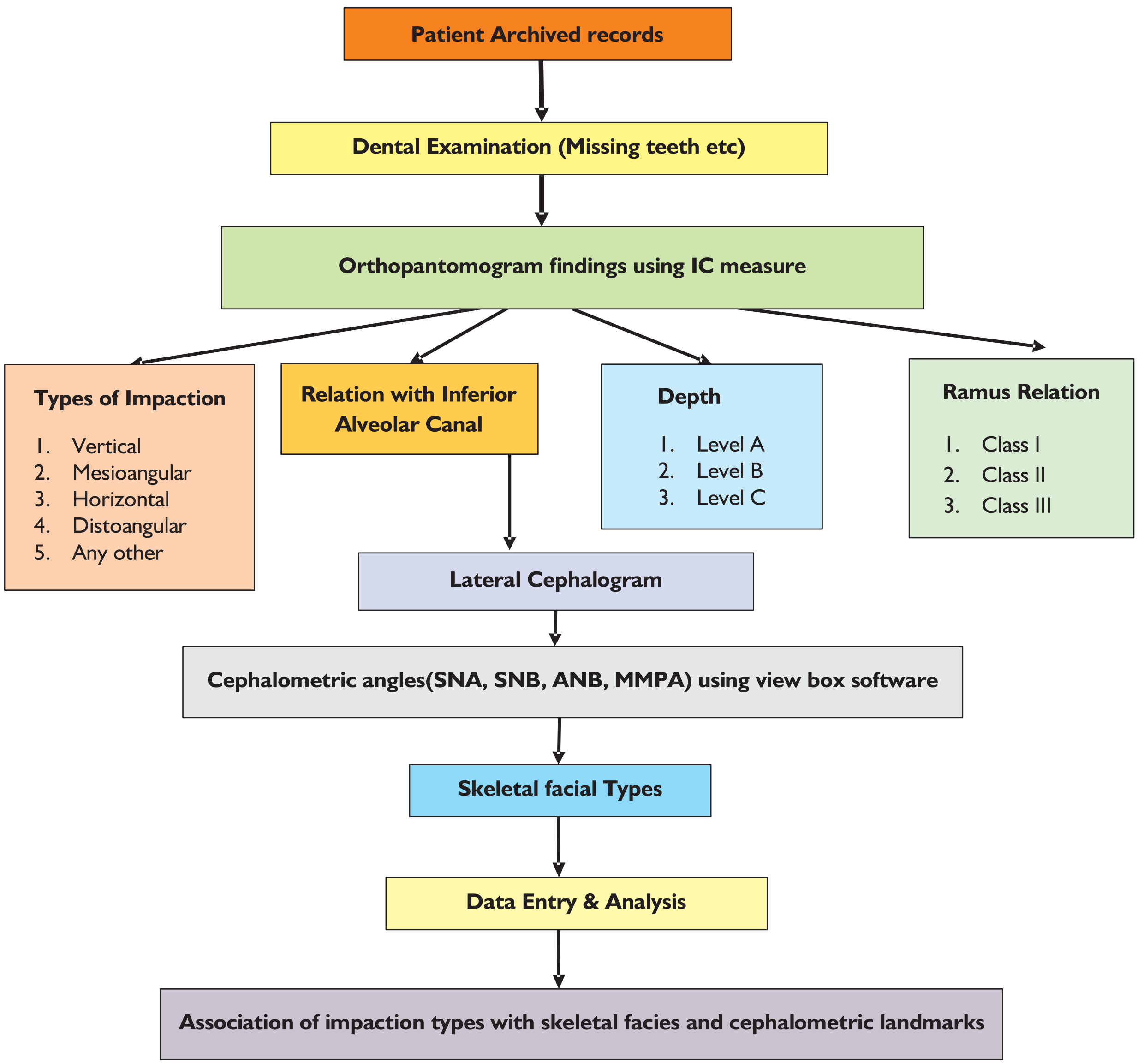

Figure 3: Flowchart showing the sequence of events

landmarks were also taken. These included SNA, SNB, ANB and MMPA. On comparing the results of our study with the ones mentioned in a meta-analysis of 14 studies carried out by Hamdan et al. of populations belonging to different ethnicities, similar findings were observed.[19] The mean values of cephalometric landmarks in our study were more or less similar to what was observed by Hamdan et al. suggesting that these landmarks do not vary much among people belonging to different ethnicities.

We did not observe any association between the impaction types and the skeletal facies. The skeletal facial classification used in our study was based on horizontal facial growth pattern. The studies carried out on similar classification showed the same results.[1] However those which were carried out on vertical growth pattern suggested otherwise. They found an association between the impacted tooth and facial skeletal type but none between the angulation of the impacted tooth with the facial skeletal type.[20] This suggests that the impacted tooth may have an impact on the vertical growth of the face however, it may not seem to be associated with the horizontal facial growth. Also, there was a significant positive correlation between the tooth angulation and the depth of the tooth suggesting deeper the teeth are more angulated. It is in accordance to Padhye et al. and it may suggest how deeply embedded the tooth is in the bone.[21] The deeper the tooth the difficult the tooth extraction and close its proximity to the ID canal. This is also supported by the results of our study where both mesial and horizontally impacted teeth were level C deep, suggesting that due to less retromolar space these types of impacted teeth are deeply embedded.

An interesting finding in our results was that there is a statistically significant but a very weak and positive correlation between the tooth angulation and the ID canal. These findings suggest that with increasing angulations of the impacted molar, the depth increases and thus the proximity of the tooth to the ID canal increases. In contrast, a study by Deshpande et al.[13] and Blaeser et al.[22] stated no correlation existed between the two factors. This can be due to the much smaller sample size taken by both the researchers in comparison to our study which lead to a different finding.

There was also a negative association between the tooth angulation and age. This explains that there is a change in the angulation of the impacted tooth with time. Our findings can be supported by another study in which a change in the tooth position in different age groups was also observed.[23] We should therefore consider re-evaluating a patient's radiograph to see the possible changes in the tooth position that occurred over a period of time. Furthermore, a weak negative correlation was found between the tooth angle and the ramus relation which is in accordance to the findings of Padhye et al. who also found a strong correlation between the tooth angulation and the ramus classification.[21] This suggests that as the angle of the impacted tooth increases the retromolar space decreases. The tooth is therefore more embedded in the bone. If mesiodistal space for the tooth to erupt is greater than the impacted tooth's diameter there are roughly 70% chances of its eruption.[21] A completely embedded tooth would require more time and special surgical techniques for its removal. A strong negative correlation was observed between the skeletal facial types and the ramus relation which means that as the ANB decreases the eruption space increases but according to Sogra et al. there is no correlation between the two variables.[1] This is because in their study facial skeletal type was determined by measuring ANB angle, wits and angle of convexity whereas in our study only ANB angle was used.

The depth of the impacted third molar was evaluated by considering the highest point of the crown of the impacted tooth with the highest portion of the adjacent second molar. From our results, most of the impacted teeth were level A deep. However, the findings are in contrast to those of Padhye et al. and Quek et al., who found level B depth to be the most common.[6,21] The disparity in result is because they included both erupted and impacted third molars in their study whereas in our study, we only considered impacted molars. Moreover, similar to what Padhye observed we also found level A to be most commonly associated with vertical types however the overall depth observed in our studies was different.[21]

The space required for the tooth to erupt must be greater than the mesiodistal width of the tooth.[24] In our study, 71.8% had class I eruption space followed by class II and III. This shows that the eruption space was more than two thirds the crown of the impacted tooth. According to a study conducted by Kim et al., on a different population with a relatively smaller size they had majority with class II eruption space.[25] The ramus relation was also significantly positively associated with the depth of the impacted tooth. This means that if there is more eruption space available and the crown of the third molar is not embedded in the bone then there is less chance for the tooth to be deeply impacted and hence will erupt into the oral cavity with ease. The ramus relation was also significantly associated with age. This signifies that with the passage of time the retromolar space increases and the chance for the tooth to be impacted lessens. This finding can be supported by other researchers who observed the same pattern in their studies.[23,26]

The proximity of the impacted tooth with the ID canal is important because it is associated with risk factors such as deflection, darkening and narrowing of the root or interruption of the white line of the canal or any narrowing and diversion of the canal and/or dark and bifid root apex. In our study we found that less than half (42%) of teeth had close proximity which is contrary to what Nakagawa observed.[27] They had great majority of impacted teeth in close proximity with the ID canal (76.7%).[27] However, as far as the individual impaction types are concerned both our study and Nakagawa's mesially impacted tooth was in close proximity to the ID canal while in our study the impaction type belonging to 'any other' category had zero proximity to the ID canal as well.[27] These findings might be useful to the maxillofacial surgeon while performing a surgical impaction as they would already know of the risk factors involved while extracting a mesially impacted molar. They will use a different surgical technique such as tooth sectioning in order to avoid any injury to the underlying nerve. We found ID canal significantly positively associated with the depth of impacted tooth suggesting that the increase in depth would result in close proximity of the tooth to the ID canal. It was contrary to what Blaeser et al. found.[21] This disparity maybe attributed to a smaller size or a different population under observation. We found a weak positive correlation between the ID canal and the ramus relation which is supported by the evidence in the literature because both the studies were carried out on the Asian population.[26] The more embedded the tooth is in the bone the deeper it is and hence has a close proximity to the ID canal. MMPA was negatively and weakly associated with the depth of the tooth and also with the ramus which means that the anterior height of the face has an association with embedment of tooth in bone and having space for its eruption. However there was no association of MMPA with the ID canal and age. Since this aspect is not much explored so further studies need to be done to determine if these findings differ in terms of ethnicities, ages or gender.

LIMITATIONS

Our study was not void of limitations. Despite the best possible efforts this study had following limitations. Although the study was based on archived records, the sample size was only 800 records due to the shortage of time. Our data collection was bicentric. It could have been multicentric but due to ongoing pandemic we had to limit it to two easily accessible hospitals. The measurements taken from the software were done by the principal investigator only. There is a chance of human error as intra-rater reliability was not tested due to time limitation. Although Viewbox and IC measure are quite convenient softwares, the measurements done were partly manual thus subjecting them to error. Although the literature suggests that for cephalometric readings, CBCT is much more reliable tool as compared to OPG. But instead of CBCT, OPG was used only OPG was available for all patients.

RECOMMENDATIONS

Based on the above mentioned discussion, following recommendations are made. Since this study was carried out on a relatively smaller sample size, a comprehensive study on a larger sample size from multicentric source may result in depicting significant association between impacted tooth angulations and facial skeletal types. For more reliable results inter and intra-rater reliability can be tested in future studies. Use of softwares which are fully automatic may yield more precise and quick results. More accurate results can be achieved by CBCT as it is a more reliable radiographic tool in detecting and measuring anatomical and cephalometric landmarks.

CONCLUSION

Our findings thus suggest that although it is difficult to determine the type of impaction the patient presents with based on their skeletal facies, some cephalometric and anatomical landmarks such as MMPA, depth, ID canal and ramus relation were found to be associated with impaction types, which may help in predicting the degree of difficulty that may be encountered during the surgical procedures. All these parameters will assist the surgeon in knowing beforehand which impaction type has more risk factors involved and hence would plan the surgery accordingly and counsel the patient regarding the timing of the surgery and the risk factors involved. They can develop new innovations in their procedures as well. Furthermore, merely knowing the type of impaction is not enough for planning surgery, a holistic overview of the relevant skeletal and cephalometric landmarks is required to develop management plan.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

SUA: Conception, acquisition, analysis and interpretation of data, drafting the manuscript, approval of the final version to be published

NB: Conception & study design, analysis and interpretation of data, drafting the manuscript, critical review, approval of the final version to be published

ZD: analysis and interpretation of data, drafting the manuscript, approval of the final version to be published

MIA: acquisition of data, drafting the manuscript, approval of the final version to be published

SJ: Acquisition, analysis and interpretation of data, drafting the manuscript, approval of the final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request

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