

Evaluation and Comparison of Third Molar Agenesis Among Indian and Malaysian Subpopulations: A Retrospective Orthopantomographic Study

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Objective: To evaluate and establish the prevalence of third molar (M3) agenesis among Indian and Malaysian subpopulations.

Material and Methods: This cross-sectional observational study was conducted as a collaborative study between Manipal College of Dental Sciences, Manipal and Melaka Medical and Dental College, Malaysia (Manipal branch). Following Ethical Committee clearance, digital orthopantomograms (OPG) of students who visited the Dental OPD of Manipal College of Dental Sciences, Manipal for orthodontic treatment or M3 disimpactions were included in the study. The data collected from the OPGs included demographic information (age and sex) and information about the presence or absence of M3. Descriptive statistics were presented as frequencies for categorical variables and as mean \pm standard deviation for age. Additionally, Fisher's exact test and chi-square test were conducted to evaluate differences within and between the two ethnic groups.

Results: Hundred OPGs each of Malaysian and Indian origin students met the inclusion criteria and were included in the study. The mean age of the study population was 15.8 ± 2.8 years (range: 13–21 years). The Indian group comprised 52 females and 48 males, while the Malaysian group included 49 females and 51 males. Among the Indian subjects, 7% had M3 present in all four quadrants, whereas 93% exhibited agenesis of M3 in at least one quadrant. Similarly, 8% of Malaysian subjects had M3 present in all four quadrants, and 92% demonstrated agenesis in at least one quadrant. Overall, M3 agenesis was observed in 77.5% of the 200 study participants.

Conclusion: M3 agenesis was highly prevalent in both Indian and Malaysian dental students, with no significant difference in overall prevalence between the two groups. Although quadrant-specific variations were observed, most comparisons did not demonstrate statistically significant intergroup differences.

Keywords: third molar, agenesis, tooth agenesis, missing tooth, congenital absence, orthopantomogram, Indian, Malaysian, students



Introduction

Agenesis of a tooth is characteristically described as the developmental absence of one or multiple teeth in the oral cavity. Tooth agenesis may be associated with genetic traits, as in craniofacial syndromes, or be present as a distinct non-syndromic entity.¹ The prevalence of non-syndromic permanent tooth agenesis other than third molars (M3) is 6.4%, whereas the prevalence of M3 agenesis is approximately 20–30%.^{1,2} Often considered vestigial in nature, third molars play a pivotal role in forensic investigations, prediction of dental age, and in regenerative medicine by virtue of their stem cell content.^{3–5}

The reason for M3 agenesis has been extensively studied, however, the higher preponderance to evolutionary mechanism or developmental mechanism is debatable.¹ Some authors have linked tooth agenesis to genes that are responsible for craniofacial morphogenesis.^{6,7} The human evolutionary process has been associated with gradual increase in the size of the brain and cranium at the expense of the size of facial structures and the number of teeth, as a sequelae of dietary and societal changes.^{8–10} The reduction in the size of tooth-bearing structures has, in turn, led to reduction in tooth size and number, a characteristic seen especially in human beings. Subsequently, higher rates of tooth agenesis have been linked to smaller facial configurations.^{11–13} The plastic response of the masticatory apparatus to evolving soft diets has further resulted in smaller jaw sizes and hence, smaller or fewer teeth.¹⁴

Consequently, tooth agenesis affects third molars most frequently, given that they remain the last teeth to erupt in the oral cavity, irrespective of jaw size, tooth size, race, and ethnicity. A relatively common finding, M3 agenesis constitutes the most frequent developmental anomaly of the permanent dentition.³ Variations in the chronology of M3 formation, calcification, and eruption have been reported among different ethnic groups. Consistent with this variability, the prevalence of M3 agenesis ranges from 0% in Tasmanians to 49% in Hungarians.^{3,15} Studies have also revealed variations in the number, arch, and side involved in M3 agenesis amongst various ethnicities.^{3,15,16}

Therefore, tracking the prevalence of M3 agenesis is not only essential for epidemiological studies but also instrumental in understanding broader evolutionary patterns over time and across different populations. Our study aims to thoroughly evaluate the prevalence of M3 agenesis in subjects from Malaysian and Indian subpopulations. In addition to assessing prevalence rates, we also intend to investigate inter-racial differences, gender predispositions, and specific patterns of agenesis within our sample. By addressing these areas, we aim to contribute to enhancing our understanding of M3 dynamics in diverse populations.

Material and Methods

This cross-sectional observational study was conducted as a collaborative study between Manipal College of Dental Sciences, Manipal and Melaka Medical and Dental College, Malaysia (Manipal branch). Both the institutions are located in Karnataka, India. The Malaysian students from Melaka College, predominantly of Chinese origin, followed a course structure that required two years of pre-clinical education in India, with subsequent clinical training undertaken in Malaysia. The study was approved by the Ethics Committee of Manipal College of Dental Sciences, which is affiliated to Kasturba Medical College and Kasturba Hospital Institutional Ethics Committee (IEC-912/2023). The study abided by the Declarations of Helsinki. The study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.¹⁷ All students provide a written informed consent for the use of their radiographs for possible research purposes at the time of their initial evaluation, in accordance with standard clinical practice. For the students below 18 years of age, written informed consent is sought from their parents by practice.

Study Design

The study included digital orthopantomograms (OPG) of students who visited the Dental OPD of Manipal College of Dental Sciences, Manipal. The inclusion criteria were:

1. Students who visited the Dental OPD for orthodontic treatment or M3 disimpactions.
2. Students of Indian (Manipal College of Dental Sciences, Manipal) or Malaysian (Melaka Medical and Dental College, Malaysia, Manipal branch) origin (as confirmed by their Identification Cards and passports).

3. Students between the age of 13 to 21 years. The lower limit was 13 years since the M3 tooth germ would be radiologically discernible at that age. The upper limit was 21 years to focus on the student population and because younger patients are less likely to forget their prior history of third molar extractions, leading to more accurate information.

The exclusion criteria of the study were:

1. History of wisdom tooth extraction or germectomy.
2. Presence of syndromic disorders, particularly those associated with dental anomalies or chronic systemic diseases.
3. Students with history of trauma or disease affecting facial development.
4. Non-standardised panoramic radiographs.
5. Students who refused to allow their diagnostic or treatment details to be used for research purposes.

Data Collection

Good quality OPGs from the radiological archives between August 2019 and August 2023 were manually reviewed by two experienced radiologists from the Department of Oral Medicine and Radiology. The OPGs were anonymized by a radiographer who was not a part of the study. The OPGs were viewed on computer monitors under optimum viewing conditions by the two radiologists independently, to reduce selection bias. The data collected from the OPGs included demographic information (age and sex) and information about the presence or absence of M3. All the data were systematically entered into a specifically drafted proforma.

Statistical Analysis

The results were subsequently transferred into a statistical software for further analysis and the study of M3 agenesis patterns. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as frequencies for categorical variables and as mean \pm standard deviation for age. Additionally, Fisher's exact test and chi-square test were conducted to evaluate differences within and between the two ethnic groups. A 95% confidence interval was used, and the level of significance was set at $p < 0.05$.

Results

A total of 2515 OPGs were manually retrieved from the radiological archives during the study period. Of these, 964 OPGs of patients with facial fractures, 4 with temporomandibular joint (TMJ) ankylosis, 91 with mandibular pathologies (benign tumors or cysts), 47 of poor radiographic quality, and 9 patients who declined participation were excluded. Consequently, 1400 good-quality OPGs were deemed eligible for evaluation. Among these, 100 OPGs of Malaysian students met the inclusion criteria. Subsequently, 100 age-matched OPGs of Indian students who met the inclusion criteria were selected for comparison. The mean age of the study population was 15.8 ± 2.8 years (range: 13–21 years).

The Indian group comprised 52 females and 48 males, while the Malaysian group included 49 females and 51 males. Among the Indian subjects, 7% had M3 present in all four quadrants, whereas 93% exhibited agenesis of M3 in at least one quadrant. Similarly, 8% of Malaysian subjects had M3 present in all four quadrants, and 92% demonstrated agenesis in at least one quadrant. Overall, M3 agenesis was observed in 77.5% of the 200 study participants. Malaysian students demonstrated a significantly higher prevalence of maxillary right M3 agenesis (83%) and mandibular left M3 agenesis (85%) compared to Indian students ($p < 0.001$ and $p = 0.037$, respectively). However, no statistically significant differences were observed between Indian and Malaysian students with respect to maxillary left M3 agenesis (67% vs 77%; $p = 0.115$) or mandibular right M3 agenesis (72% vs 81%; $p = 0.133$). Additionally, there was no significant difference in the overall prevalence of M3 agenesis between Indian (93%) and Malaysian students (92%) ($p = 0.788$). Representative OPGs demonstrating M3 agenesis in the first (Figure 1A), second (Figure 1B), third (Figure 1C), and fourth quadrants (Figure 1D) are shown in Figure 1. A comparative analysis of M3 agenesis between the two ethnic groups is presented in Table 1.

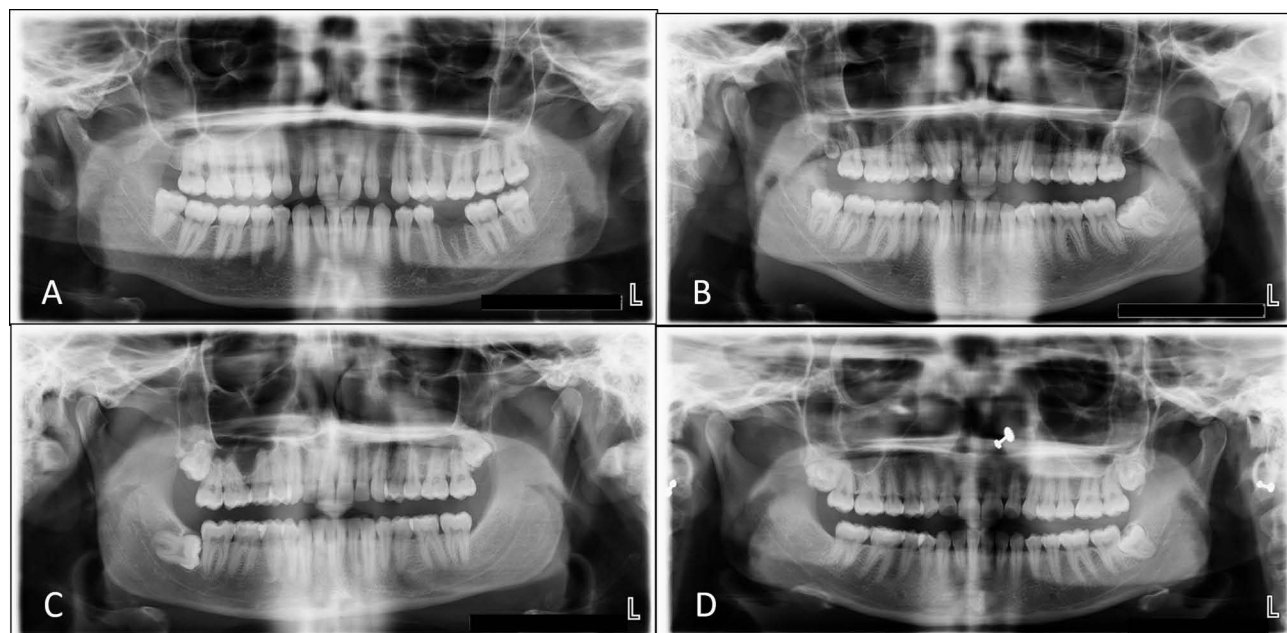


Figure 1 (A) OPG representing agenesis of the third molar in the first quadrant; (B) OPG representing agenesis of the third molar in the second quadrant; (C) OPG representing agenesis of the third molar in the third quadrant; (D) OPG representing agenesis of the third molar in the fourth quadrant [the alphabetical letter (L) indicates the left side of the OPG].

Among the Indian subpopulation (Table 2), no statistically significant differences were observed between males and females in the distribution of agenesis with respect to maxillary right (71.4% vs 52.9%; $p = 0.057$), maxillary left (73.5% vs 60.8%; $p = 0.177$), mandibular left (71.4% vs 74.5%; $p = 0.729$), or mandibular right third molars (73.5% vs 70.6%; $p = 0.748$). However, females (79.6%) demonstrated a significantly higher prevalence of bilateral maxillary M3 agenesis compared to males (60.8%) ($p = 0.04$). No significant difference was noted in bilateral mandibular M3 agenesis between

Table 1 Comparison of Third Molar Aggenesis Between Indian and Malaysian Subpopulations

		Country				P-value
		Indian		Malaysian		
		N	%	N	%	
Maxillary right third molar	Absent	62	62.0%	83	83.0%	<0.001*
	Present	38	38.0%	17	17.0%	
Maxillary left third molar	Absent	67	67.0%	77	77.0%	0.115
	Present	33	33.0%	23	23.0%	
Mandibular left third molar	Absent	73	73.0%	85	85.0%	0.037*
	Present	27	27.0%	15	15.0%	
Mandibular right third molar	Absent	72	72.0%	81	81.0%	0.133
	Present	28	28.0%	19	19.0%	
Bilateral maxillary third molar	Absent	70	70.0%	84	84.0%	0.019*
	Present	30	30.0%	16	16.0%	

(Continued)

Table 1 (Continued).

		Country				P-value
		Indian		Malaysian		
		N	%	N	%	
Bilateral mandibular third molars	Absent	85	85.0%	89	89.0%	0.4
	Present	15	15.0%	11	11.0%	
All Quadrants	Absent	93	93.0%	92	92.0%	0.788
	Present	7	7.0%	8	8.0%	

Notes: Chi-square test; *denotes statistical significant.

Table 2 Comparison of Third Molar Agenesis Between Male and Female Indian Subpopulation

Indian		Gender				P-value
		Male		Female		
		N	%	N	%	
Maxillary right third Molar†	Absent	35	71.4%	27	52.9%	0.057
	Present	14	28.6%	24	47.1%	
Maxillary left third molar†	Absent	36	73.5%	31	60.8%	0.177
	Present	13	26.5%	20	39.2%	
Mandibular left third molar†	Absent	35	71.4%	38	74.5%	0.729
	Present	14	28.6%	13	25.5%	
Mandibular right third molar†	Absent	36	73.5%	36	70.6%	0.748
	Present	13	26.5%	15	29.4%	
Bilateral maxillary third molar†	Absent	39	79.6%	31	60.8%	0.04*
	Present	10	20.4%	20	39.2%	
Bilateral mandibular third molar†	Absent	43	87.8%	42	82.4%	0.449
	Present	6	12.2%	9	17.6%	
All Quadrants‡	Absent	48	98.0%	45	88.2%	0.112
	Present	1	2.0%	6	11.8%	

Notes: †Chi-square test; ‡Fisher's exact test; *denotes statistically significant.

males and females (87.8% vs 82.4%; $p = 0.449$). Additionally, overall M3 agenesis did not differ significantly between males (98%) and females (88.2%) ($p = 0.112$). An OPG representing agenesis of both upper third molars (Figure 2A) and both lower third molars (Figure 2B) is shown in Figure 2.

A similar gender-based analysis was conducted among Malaysian students (Table 3). No statistically significant differences were found between males and females in the distribution of agenesis for maxillary right (79.6% vs 86.3%; $p = 0.374$), maxillary left (73.5% vs 80.4%; $p = 0.411$), mandibular left (83.7% vs 86.3%; $p = 0.716$), or mandibular right third molars (77.6% vs 84.3%; $p = 0.389$). Likewise, no significant differences were observed in bilateral maxillary (81.6% vs 86.3%; $p = 0.527$) or bilateral mandibular M3 agenesis (85.7% vs 92.2%; $p = 0.303$) between males and

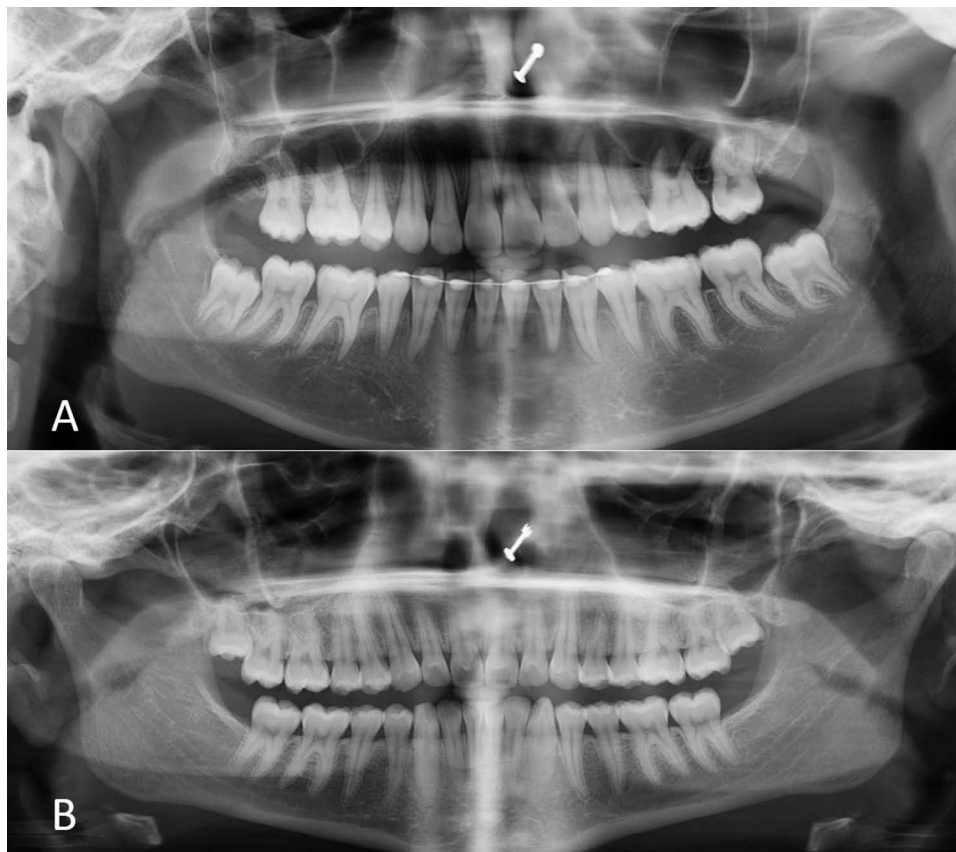


Figure 2 (A) OPG representing agenesi of bilateral upper third molars; **(B)** OPG representing agenesi of bilateral lower third molars.

females. Overall, M3 agenesi also did not differ significantly between males (89%) and females (94.1%) ($p = 0.483$). An OPG representing agenesi of all third molars is shown in [Figure 3](#).

In summary, agenesi of mandibular left M3 was highest in both the Malaysian and Indian subpopulations. The prevalence of bilateral maxillary and bilateral mandibular M3 agenesi was higher in the Malaysian subpopulation as compared to the Indian population. Overall, males were more affected by M3 agenesi in the Indian subpopulation, whereas females were affected more in the Malaysian subpopulation. However, the difference was not statistically significant.

Table 3 Comparison of Third Molar Agenesi Between Male and Female Malaysian Subpopulation

Malaysian		Gender				P-value
		Male		Female		
		N	%	N	%	
Maxillary right third molar†	Absent	39	79.6%	44	86.3%	0.374
	Present	10	20.4%	7	13.7%	
Maxillary left third molar†	Absent	36	73.5%	41	80.4%	0.411
	Present	13	26.5%	10	19.6%	
Mandibular left third molar†	Absent	41	83.7%	44	86.3%	0.716
	Present	8	16.3%	7	13.7%	

(Continued)

Table 3 (Continued).

Malaysian		Gender				P-value
		Male		Female		
		N	%	N	%	
Mandibular right third molar†	Absent	38	77.6%	43	84.3%	0.389
	Present	11	22.4%	8	15.7%	
Bilateral maxillary third molar†	Absent	40	81.6%	44	86.3%	0.527
	Present	9	18.4%	7	13.7%	
Bilateral mandibular third molar†	Absent	42	85.7%	47	92.2%	0.303
	Present	7	14.3%	4	7.8%	
All Quadrants‡	Absent	44	89.8%	48	94.1%	0.483
	Present	5	10.2%	3	5.9%	

Notes: †Chi-square test; ‡Fishers exact test.

Discussion

The present study aimed to evaluate the patterns of M3 agenesis in two distinct ethnic groups - Malaysian and Indian - without the presence of agenesis in any other permanent teeth. Aggenesis, or congenitally missing teeth, refers to the failure of a tooth to develop during its expected stages of growth and development. This condition is commonly termed hypodontia.² The M3, which develops entirely postnatally, is the last tooth to erupt across all ethnic groups, typically between 13 and 19 years of age, although variations in eruption timing and sequence have been reported among different populations.^{3,15} Tooth development can be influenced by multiple factors, including environmental influences, systemic diseases, genetic polymorphisms, and exposure to teratogens, which may affect tooth size, morphology, position, or even result in complete agenesis.⁴ Furthermore, masticatory function and dietary patterns play a significant role in lateral and inferior periosteal bone growth, potentially exerting a decelerating effect on overall craniofacial development.^{14,18,19} Yamada and Kimmel et al demonstrated through experimental studies that rats fed a soft diet exhibited a significant reduction in lateral and inferior periosteal bone growth of the mandibular ramus, along with decreased condylar elongation.²⁰ Masticatory muscle function also influences transverse craniofacial growth; reduced functional loading may result in decreased dental arch width, thereby increasing the likelihood of M3 impaction or agenesis.²¹



Figure 3 OPG representing agenesis of third molars in all four quadrants [the alphabetical letter (L) indicates the left side of the OPG].

Given that the M3 is the last tooth to develop, it is not surprising that developmental abnormalities affecting this tooth are relatively common.⁶ To date, only a limited number of mutations in the MSX1 and PAX9 genes have been definitively associated with severe forms of hypodontia in humans. PAX9 encodes a transcription factor expressed in the dental mesenchyme during the initiation, bud, cap, and bell stages of odontogenesis.²² The protein products of this gene function as transcription factors that mediate epithelial–mesenchymal interactions, which are essential for establishing the odontogenic potential of the mesenchyme. Expression of PAX9 in the mesenchyme serves as a marker for future sites of tooth development. Mutations in PAX9 have been linked to autosomal dominant forms of oligodontia, defined as the congenital absence of more than six teeth in humans.^{22,23}

In a study conducted by Jacob et al¹⁶ involving 734 Malaysian subjects, 192 individuals (26.2%) exhibited radiographic evidence of one or more missing third molars. Among the different ethnic groups studied, the highest prevalence of M3 agenesis was observed in Malaysian Chinese (32%), followed by Malays (25.5%) and Indians (21.4%). Agenesis of one or more third molars was more prevalent in females (27.5%). These findings are broadly consistent with the results of the present study, wherein females (86.3%) were more frequently affected than males (81.6%) among Malaysians. However, no statistically significant gender-based difference was observed within the Indian cohort. This observation may be attributed to the progressive transition toward softer, processed foods in contemporary dietary practices.^{18,19} In contrast, research conducted by Sandhu et al, George et al, Patil et al and Jadhav et al revealed higher prevalence of M3 agenesis among males as compared to females.^{24–27}

Overall, a slightly higher prevalence of M3 agenesis was noted in the Indian subpopulation (93%) when compared to the Malaysian subpopulation (92%) in the current study, which was not statistically significant. These findings are consistent with those reported by Ren et al,²⁸ who evaluated the prevalence of congenitally absent third molars among South Indian and Malaysian populations. Their study concluded that congenital absence was more common among South Indians as compared to Malaysians. However, among the subpopulations, Malaysians demonstrated higher prevalence of M3 agenesis in males (28%) as compared to females (20%), while the Indian group demonstrated higher prevalence in females (64%) as compared to males (48%). This finding contradicts the findings of our study, wherein Indian males (98%) and Malaysian females (94.1%) were more affected by M3 agenesis.

M3 impaction are most common among young adults of age group 18 to 21 years. Studies have shown that with increasing age, impaction of the M3 decreases.^{29,30} Impacted third molars are associated with numerous odontogenic pathologies such as cyst and tumours. Hence, M3 agenesis attributes to the reduced incidence of such pathologies.^{31,32} Partially or completely impacted M3 causes proximal caries on the distal surface of the second molar, which increases the burden of expense of restoration or root canal treatment.^{33,34} Pericoronal inflammation due to infection associated with M3 adds to the insurance burden and increased expenses for surgical removal.³⁵ Erupted third molars can be oddly positioned in the arches contributing to development of oral traumatic ulcers, traumatic fibromas and frictional keratosis.³⁶

This is one of the few studies evaluating the prevalence of M3 agenesis among Malaysian and Indian subpopulations. It demonstrates evolutionary M3 agenesis within the Indian and Malaysian subpopulations, which may contribute to reducing the burden of M3-related pathologies through appropriate patient education. This information can be effectively communicated to patients using a simple OPG. A major limitation of the study was the inclusion of a closed cohort of Malaysian and Indian students undergoing orthodontic treatment or M3 disimpaction surgery, which may not be representative of the broader Malaysian or Indian populations. The predominance of Chinese Malaysians in the Malaysian subpopulation may have further introduced selection bias. Therefore, we recommend conducting further studies with larger and more diverse populations to validate and strengthen the hypothesis of M3 agenesis.

Conclusion

In summary, M3 agenesis was highly prevalent in both Indian and Malaysian dental students, with no significant difference in overall prevalence between the two groups. Although quadrant-specific variations were observed, most comparisons did not demonstrate statistically significant intergroup differences. The progressive trend of tooth agenesis may have significant implications for age estimation studies, forensic identification methods, and medico-legal cases that rely on third molars. Furthermore, M3 agenesis could substantially influence the management and treatment planning of orthodontic patients. Nevertheless, further large-scale studies are necessary to determine the true prevalence and overall impact of M3 agenesis.

Ethical Clearance

The study was approved by the Ethics Committee of Manipal College of Dental Sciences, which is affiliated to Kasturba Medical College and Kasturba Hospital Institutional Ethics Committee (IEC-912/2023). The study abided by the Declarations of Helsinki.

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Disclosure

The authors report no conflicts of interest in this work.

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