

Phenotypes of Enamel Hypomineralization and Molar Incisor Hypomineralization in Permanent Dentition: Identification, Quantification and Proposal for Classification

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Objectives: To report the extent, pattern, clinical presentation and phenotypes of enamel hypomineralization in permanent dentition **Study Design:** This cross sectional observational study recruited a random sample of 1726, 12-16 year olds. Enamel hypomineralization was scored on all teeth by a calibrated examiner using the EAPD 2003 criteria. Proportions of affected subjects (prevalence) with a minimum of one hypomineralization and Molar Incisor Hypomineralization (MIH) were calculated. Proportions of following phenotypes were quantified i.e. MH (only FPM hypomineralization), M+IH (concomitantly affected FPMs and permanent incisors without affecting any other tooth in the arch), MIHO (hypomineralization affecting at least one of the canines, premolars or 2nd molars and simultaneously including at least one FPM), IH (only permanent incisor's hypomineralization) and NoFPM (hypomineralization affecting at least one of the canines, premolars and 2nd molars but not FPM; incisors can be affected concomitantly). A comparative evaluation of extent and severity of enamel hypomineralization was performed amongst various phenotypes. Statistical measures employed t-test, chi square tests and ANOVA. **Results:** Overall prevalence of affected subjects was 13.21% (228/1726) and 9.79% (169/1726) for enamel hypomineralization and MIH respectively. A total of 4.36±3.45 teeth/subject and 6.01±5.20 surfaces/subject were found to be affected with enamel hypomineralization. Most prevalent phenotype was M+IH while the least prevalent was IH. Maximum severity i.e. number of affected surfaces and surfaces with PEB were reported for MIHO ($p < 0.001$). **Conclusion:** Enamel hypomineralization can manifest in any tooth in five phenotypic variations in permanent dentition with varying extent and severity.

Key words: Enamel defects, enamel hypomineralization, molar incisor hypomineralization, MIH phenotypes, MIH severity

INTRODUCTION

Enamel hypomineralization is a qualitative defect of enamel owing to poor mineralization of developing enamel, identified visually as a creamy-white/yellowish/yellowish-brown opacity with/without post-eruptive breakdown (PEB).¹ Molar incisor hypomineralization (MIH) is a type of enamel hypomineralization defined as hypomineralization of one or more first permanent molars (FPMs) and frequently involving permanent incisors (PIs) as well.² According to European Academy of Paediatric Dentistry (EAPD 2003) diagnostic criteria MIH is diagnosed if either of demarcated opacity, enamel breakdown or atypical restoration is identified on any of the FPMs.³ The index teeth include FPMs and PIs while rest of the teeth are usually not scored.

Though following introduction of EAPD 2003 criteria reporting of MIH has got uniform and standardized, data on extent and clinical presentation of enamel hypomineralization of teeth other than index teeth (FPMs and PIs) are lacking. Employing the EAPD 2003 criterion which is currently an accepted and standard diagnostic criterion for recording and reporting MIH, only two phenotypes

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i.e. MH and M+IH can be reported. Another phenotype reported in permanent dentition is 'Idiopathic incisor hypomineralization'⁴ i.e. enamel hypomineralization affecting solely PIs. However, enamel hypomineralization can manifest in other teeth i.e. primary teeth and permanent canines, premolars and second molars as well.^{3,5-10} In primary dentition, few reports have been published on hypomineralized second primary molars (HSPMs).⁵⁻⁹ Term 'deciduous molar hypomineralization' (DMH) has been proposed to describe this phenotype.⁵ Concomitant involvement of primary and permanent molars has also been reported.^{9,9} Lygidakis et al.³ recommended that to report the full pattern of manifestation of enamel hypomineralization, all teeth of entire dentition should be scored.

Recently, the GINIplus-10 study group from Germany reported the extent of phenotypes of enamel hypomineralization in mixed dentition.⁹ This study group identified and described few phenotypes of enamel hypomineralization i.e. hypo-mineralization of primary molars, MH and M+IH. However, reports of extent and pattern of manifestation of enamel hypomineralization on other teeth of permanent dentition employing EAPD 2003 criteria are lacking.

With all these background facts, the present study was planned to report the extent, pattern, clinical presentation of enamel hypomineralization in permanent dentition. Further objectives of the present study were to identify and quantify the phenotypes of enamel hypomineralization and inter-compare the extent and severity of enamel hypomineralization in identified phenotypes.

The following phenotypes were identified on the basis of a pilot observation:

- MH: hypomineralization affecting only FPMs without affecting any other tooth in the dentition.
- IH: hypomineralization affecting only PIs without affecting any other tooth in the arch; excluding those with a history of trauma/infection to primary incisors.
- M+IH: hypomineralization affecting FPMs and PIs simultaneously, but not any other tooth in the dentition.
- MIHO: hypomineralization affecting FPMs and at least one of the canines, premolars or 2nd molars. PIs may be affected simultaneously. Those with a history of trauma/infection to primary teeth were excluded.
- NoFPM: hypomineralization affecting at least one of the canines, premolars or 2nd molars but not FPMs. PIs may be affected simultaneously. Those with a history of trauma/infection to primary teeth were not considered.

Another objective was to suggest a classification scheme for enamel hypomineralization based on the observed phenotypes and their clinical characteristics.

MATERIALS AND METHOD

The present study was approved by institutional ethical committee and review board.

The study population comprised of 12-16 year old school children of optimally fluoridated area (1 ppm) Gautam Budh Nagar, Uttar Pradesh, India¹⁰. A random selection of schools was done to ensure entire geographical coverage of study location. The targeted sample size was 2000. Permission to conduct oral examination in schools was sought by writing to school's administrative authorities.

Parental written consents were obtained by school authorities. Cohorts of children born in years 1996-2002 and studying in respective schools in academic years 2012-2013 and 2013-2014 were enrolled. Schools for children with special health care needs were not included.

Inclusion criteria were 12-16 years of age, full complement of erupted permanent dentition (except 3rd molars), positive parental informed consent and presence in the school on the day of examination. Exclusion criteria were developmental defects other than enamel hypomineralization i.e. amelogenesis imperfecta, dentinogenesis imperfecta, tetracycline staining or diffuse hypoplastic lesions (i.e. fluorosis). We did not include children with grossly broken down or missing teeth where causes of breakage or loss could not be determined.

The entire examination was conducted by a single examiner experienced in diagnosis of enamel hypomineralization. The examiner has been calibrated earlier for a previous study and details of calibration have been published elsewhere.¹² The kappa statistics for intra-examiner reliability were excellent i.e. 0.98.¹³ The clinical examinations were performed in school premises with a portable source of artificial light. All children were instructed to brush their teeth prior to examination. Any debris if remaining was removed either by cotton or blunt ended probe during examination. Plain mouth mirrors and blunt ended probes were used for examination.

All erupted teeth were scored for enamel hypomineralization using EAPD 2003 criteria.³ Surfaces examined included occlusal, buccal, lingual/palatal. Only those defects with size ≥ 2 mm were recorded. Extent of every defect was measured by recording surface area affected by defect. Defects were graded as Defect 1 (<1/3rd of tooth surface), Defect 2 (involving 1/3rd to 2/3rd of tooth surface), Defect 3 (>2/3rd of tooth surface).

The entire data were entered on pre-printed proforma which had a provision to record demographic details, affected teeth, affected surfaces, type of defect (opacity/PEB/atypical restoration) and extent of defects (defect 1/defect 2/defect 3).

Data management and statistical methods

From the proforma, data were first entered into Microsoft office Excel spreadsheet (Microsoft office®, Microsoft®, Redmond, Washington, USA) and then transported to SPSS® version 21 (IBM, New York, USA) for statistical analysis.

Descriptive data were expressed as mean \pm SD and/or proportions/percentages for all affected subjects with enamel hypomineralization as well as for individual phenotypes i.e. MH, M+IH, IH, MIHO and NoFPM. The descriptive data were expressed for various parameters i.e. total number of affected teeth, affected surfaces, affected occlusal/buccal/lingual surfaces, surfaces with defect 1/2/3, creamy white opacities, yellowish brown opacities, surfaces with PEB, atypical restorations.

The comparative inter-group statistics were computed for above mentioned parameters using ANOVA and Post-hoc tests. P value of ≤ 0.05 was considered to be significant and ≤ 0.01 was considered to be highly significant.

RESULTS

Overall rate of participation was 90.8% (1816/2000). Finally, we were able to examine 1726 subjects as rest of the subjects were absent on the day of examination. Thus, final participation rate was 86.3%.

An overall prevalence of 13.21% (228/1726) was reported for enamel hypomineralization. Prevalence of molar incisor hypomineralization (MIH) i.e. FPM hypomineralization was 9.79% (169/1726). It is to be noted that MIH comprised of phenotypes MH, M+IH and MIHO.

Out of affected subjects with enamel hypomineralization (n = 228), proportions of reported phenotypes were 27.63% (63/228), 31.14% (71/228), 15.35% (35/228), 11.84% (27/228) and 14.04% (32/228) for MH, M+IH, MIHO, IH and NoFPM respectively.

Significantly greater number of maxillary teeth were affected compared to mandibular teeth (p=0.031; Figure 1). Most commonly affected teeth were FPMs while canines were least commonly affected (Figure 1a & 1b). Most commonly affected surfaces were buccal surfaces while lingual surfaces were least commonly affected (p = 0.000). Commonest lesion was creamy white opacity (p = 0.000) and PEB was observed in 41.23% (94/228) of affected subjects.

Subjects presenting with phenotype MIHO exhibited highest number of affected teeth and surfaces, while the minimum magnitudes of these parameters were observed in subjects with phenotype IH (p=0.000). Most extensive defects (defect 3; >2/3rd of surface area involvement) were reported in phenotype M+IH (p= 0.071). In all of the reported phenotypes, creamy white opacities outnumbered yellowish brown opacities (p=0.000). Maximum numbers of yellowish brown opacities were reported in phenotypes M+IH and MIHO (p=0.000). PEB was significantly more often observed in phenotype MIHO (p = 0.000).

In phenotype MH, almost equal involvement of maxillary and mandibular arches was seen; while in phenotype IH, greater predilection was seen for maxillary arch. In phenotype M+IH, almost equal predilection was seen for both the arches, but mandibular FPMs were more frequently involved than maxillary FPMs. In phenotype MIHO, almost any tooth could be found to be affected. Most commonly affected were premolars followed by FPMs while least commonly affected were canines. In phenotype MIHO, incisors and second molars were almost equally affected. In phenotype NoFPM, most commonly affected teeth were premolars while the least commonly affected teeth were canines.

Table 1: Overall defect characteristics of Enamel Hypomineralisation in study population†

Characteristic	Mean±SD (n= 228)	95% Confidence Interval for Mean	
		Lower Bound	Upper Bound
Affected permanent teeth	4.36±3.45	3.91	4.81
Affected permanent surfaces	6.01±5.20	5.33	6.69
Affected Occlusal surfaces	2.04±2.31	1.74	2.35
Affected Buccal surfaces	3.54±3.40	3.10	3.99
Affected Lingual surfaces	0.43±1.09	0.29	0.58
Surfaces with <1/3 rd of area involvement (Defect 1)	3.39±4.10	2.85	3.92
Surfaces with 1/3 rd to 2/3 rd of area involvement (Defect 2)	2.19±3.77	1.70	2.68
Surfaces with >2/3 rd of area involvement (Defect 3)	0.44±2.41	0.12	0.75
Creamy white opacities	4.60±4.67	3.99	5.21
Yellowish brown opacities	1.41±2.04	1.14	1.67
Post eruptive breakdown (PEB)	1.15±1.78	0.92	1.39

†data expressed for mean values/subject

Table 2: Intergroup statistics: Defect characteristics

Characteristics (Mean±SD)	Groups					p value†
	MH n = 63	M+IH n= 71	IH N = 27	MIHO N = 35	NoFPM N = 32	
Affected teeth	2.57±1.27	4.86±1.88	1.52±0.80	9.74±4.01	3.31±3.17	0.000*
Affected surfaces	4.63±3.47	7.00±4.95	1.63±0.97	11.63±5.74	4.09	0.000*
Surfaces with <1/3 rd of area involvement (Defect 1)	3.06±3.72	3.06±3.80	0.96±0.94	7.43±5.37	2.38±2.27	0.000*
Surfaces with 1/3 rd to 2/3 rd of area involvement (Defect 2)	1.48±2.56	2.82±4.42	0.59±.93	3.94±5.39	1.63±2.58	0.001*
Surfaces with >2/3 rd of area involvement (Defect 3)	0.10±0.43	1.13±4.18	0.07±0.39	0.26±0.85	0.09±0.30	0.071
Creamy white opacities	3.86±3.63	4.97±4.84	1.44±1.01	9.57±5.14	2.47±2.84	0.000*
Yellowish brown opacities	0.76±1.17	2.03±2.26	0.19±0.56	2.06±2.62	1.63±2.23	0.000*
Post eruptive breakdown (PEB)	0.60±1.07	1.46±1.69	0.19±0.56	2.17±2.64	1.25±1.93	0.000*

§data expressed for mean values/subject †calculated on the basis of ANOVA; *highly significant p value

DISCUSSION

The final response rate in our study was good i.e. 86.3%. Thus, our sample can be considered to be representative of targeted study population.

The diagnosis of enamel hypomineralization was carried out employing recommended EAPD 2003 criteria (in wet conditions using artificial light source) which is currently accepted, validated and standard criteria for reporting of MIH/enamel hypomineralization.³ All examinations were conducted by a single experienced examiner with excellent intra-examiner agreement (kappa value=0.98).¹³ Thus, our diagnostic criteria should remain reliable and valid.

The proportion of children with enamel hypomineralization was 13.21% in present study. This finding is similar to the prevalence of enamel hypomineralization reported from Sweden,¹ Lithuania,¹⁴ and New Zealand.^{15,16} However, much higher prevalence rates have

been reported from most of the studies¹⁷⁻¹⁹ and few of them reported a prevalence rate of as high as 60%.²⁰

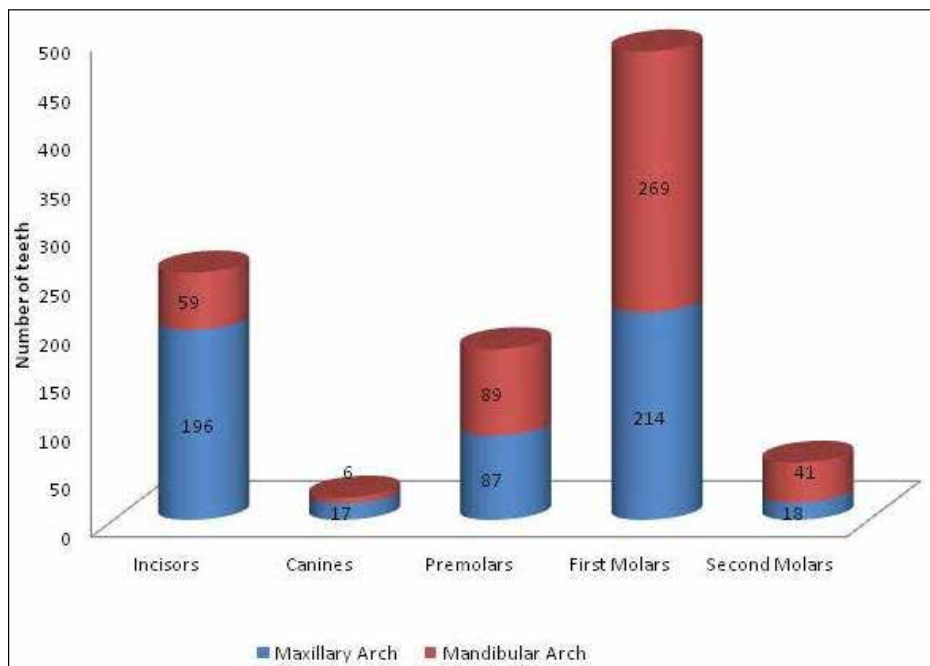
The prevalence rate of 9.79% for MIH is similar to prevalence reported from western India²¹ (9.2%) but differs from the prevalence reported from northern India¹² (6.3%). Although the present study was also conducted in northern India and the diagnostic criteria were similar to those employed by Mittal et al.,¹² the prevalence rate in the present study was higher. The explanation may lie with the fact that Mittal et al.¹² employed younger subjects (6-9 years of age) when all index teeth were not erupted and could have under-reported the prevalence rate.

Widely varying prevalence rates (2.8²²-40.2%²³) of MIH have been reported from across the globe. These wide variations have been attributed to either of the following reasons; real differences in prevalence rates, varying diagnostic criteria employed prior to introduction of EAPD 2003 criteria, recruitment of varying age

Table 3: Pattern of distribution of enamel hypomineralization as per tooth type amongst various phenotypes

Phenotype	Type of affected tooth; n (%)										Total
	Maxillary Incisors	Mandibular Incisors	Maxillary Canines	Mandibular Canines	Maxillary Premolars	Mandibular Premolars	Maxillary FPMs	Mandibular FPMs	Maxillary 2nd Molars	Mandibular 2nd Molars	
MH	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	78 (48.15)	84 (51.85)	0 (0)	0 (0)	162 (100)
M+IH	111 (32.17)	36 (10.43)	0 (0)	0 (0)	0 (0)	0 (0)	80 (23.19)	118 (34.20)	0 (0)	0 (0)	345(100)
MIHO	23 (6.74)	19 (5.57)	10 (2.93)	3 (0.88)	69 (20.23)	65(19.06)	44 (12.90)	66 (19.35)	18 (5.28)	24 (7.04)	341(100)
IH	38 (92.68)	3 (7.32)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	41(100)
NoFPM	25 (23.58)	0 (0)	7 (6.60)	3 (2.83)	27 (25.47)	27 (25.47)	0 (0)	0 (0)	0 (0)	17 (16.04)	106(100)

Figure 1: Distribution of defects amongst maxillary and mandibular arches and by tooth type



groups or poor/no calibration of examiner. However, the prevalence of MIH reported in our study is similar to prevalence reported from Greece,¹⁹ Lithuania,¹⁴ Turkey,²⁴ Netherlands²⁵ and New Zealand.²⁶ Although most the Asian studies have reported different prevalence rates i.e. 2.8 % in Hong Kong,²² 17.6 % in Jordan²⁷ and 18.6 % in Iraq⁴; a recent report from Singapore has reported almost similar prevalence rate of 12.5%.⁸

Almost equivalent proportions of phenotypes MH (27.63%) and M+IH (31.14%) were observed, which were most frequently reported phenotypes in the study population. Least commonly reported phenotype was IH (11.84%). The comparison of this data with previous reports is difficult as few of the phenotypes reported in this study (MIHO and NoFPM) have not been reported earlier as the teeth examined in these phenotypes are not index teeth according to EAPD 2003 criteria.

Most commonly reported phenotypes in the previously published papers are MH and M+IH. Few of the Asian studies^{4,12} have reported almost equivalent proportions of these two phenotypes in individuals affected with MIH; a finding similar to our study. However, most of the studies^{14,19,21,27,28} have reported that M+IH phenotype is more prevalent compared to MH phenotype.

The phenotype NoFPM reported in this study constituted a sizeable proportion i.e. 14.04% of enamel hypomineralization and the prevalence of this phenotype was 1.85% in study population. As stated above that the prevalence of enamel hypomineralization in many population groups is much higher than reported by us,¹⁷⁻²⁰ much higher prevalence of phenotype NoFPM may be expected in those populations. Thus, recording of only index teeth would lead to underestimation of enamel hypomineralization and treatment needs owing to hypomineralization. With the findings of this study it is expected that all teeth of dentition would be examined in future studies to ensure estimating the full clinical impact of enamel hypomineralization.

The greatest extent (measured as mean number of affected teeth and/or surfaces) and greatest severity (measured as mean number of surfaces with PEB) was reported for phenotype MIHO followed by M+IH. Although comparisons with previously published data is difficult as this is the first study to report full extent of enamel hypomineralization in permanent dentition employing EAPD 2003 criteria, it is still possible for some parameters. Most of the previously published literature^{4,12,23,29} has reported greater severity of phenotype M+IH compared to phenotype MH and this fact corroborates with the findings of the present study.

Previous reports have stated that severity of hypomineralization defects i.e. defect type and extent increased with increase in number of affected teeth/surfaces.^{4,12,21,27,30,31} Our study also substantiates this fact as greater severity was reported for phenotypes exhibiting greater number of affected teeth/surfaces.

In previously published literature employing EAPD 2003 criteria for reporting of MIH, it is possible that phenotype M+IH included phenotype MIHO as well as teeth other than index teeth were usually not scored. Since, only FPMs and PIs were scored, it is also possible that lesser extent and severity of phenotype MIHO (though reported as phenotype M+IH) might have been reported. This fact again underlines the importance of examining all teeth in dentition to record the full extent and severity of enamel hypomineralization.

Another interesting finding was greater severity and extent of enamel hypomineralization in phenotype NoFPM compared to phenotype MH. This phenotype has not been reported earlier as classically described index teeth in MIH definition i.e. FPMs are not affected in this phenotype. Nevertheless, not overemphasizing, this finding has very important implications for future epidemiological research of enamel hypomineralization and again calls for scoring all teeth of dentition in future studies.

Suggested age groups for screening of enamel hypomineralization

Enamel hypomineralization is a dynamic condition with a tendency of hypomineralization defects to transform into more severe defects i.e. sound opacities may progress to PEB.³² This fact underlines the importance of early diagnosis as well as management. In light of the previously published literature as well the findings of present study, it is obvious that most commonly affected teeth are FPMs and PIs.¹⁰ Thus, the appropriate age of screening for enamel hypomineralization should be when FPMs and PIs are fully erupted i.e. 8 years. Since, almost any tooth in the dentition can be affected,³⁻¹⁰ next age of examination should be when full complement of permanent dentition has been erupted i.e. 13-14 years. At this age, all teeth should be examined to record the full extent as well as severity of enamel hypomineralization.

The present study is first study to report the extent of enamel hypomineralization in full complement of permanent dentition. It is suggested that future studies in various population groups should attempt to report the tooth-wise extent of enamel hypomineralization in full complement of permanent dentition.

Figure 2: Distribution of defects by individual tooth types

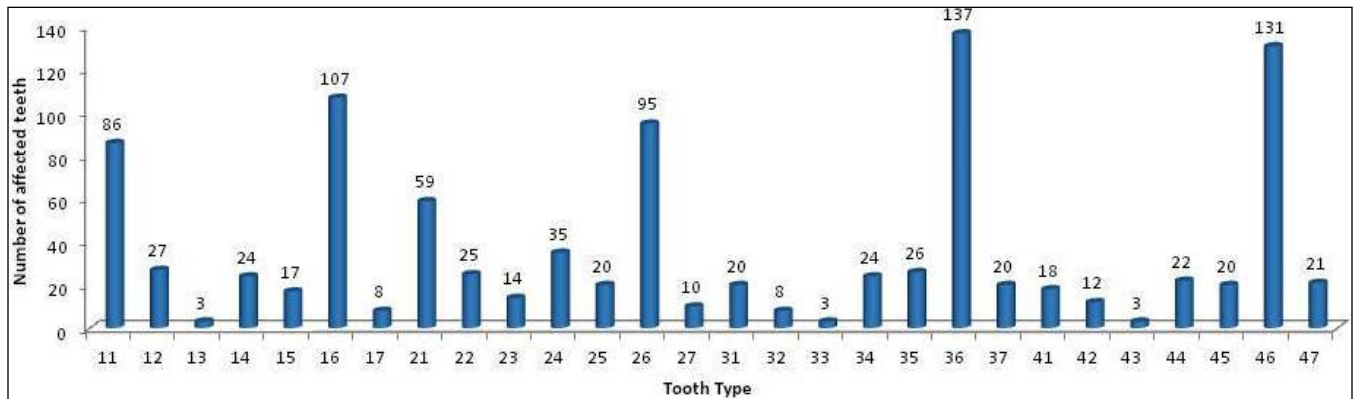


Figure 3: Distribution of defects by individual tooth types amongst different phenotypes

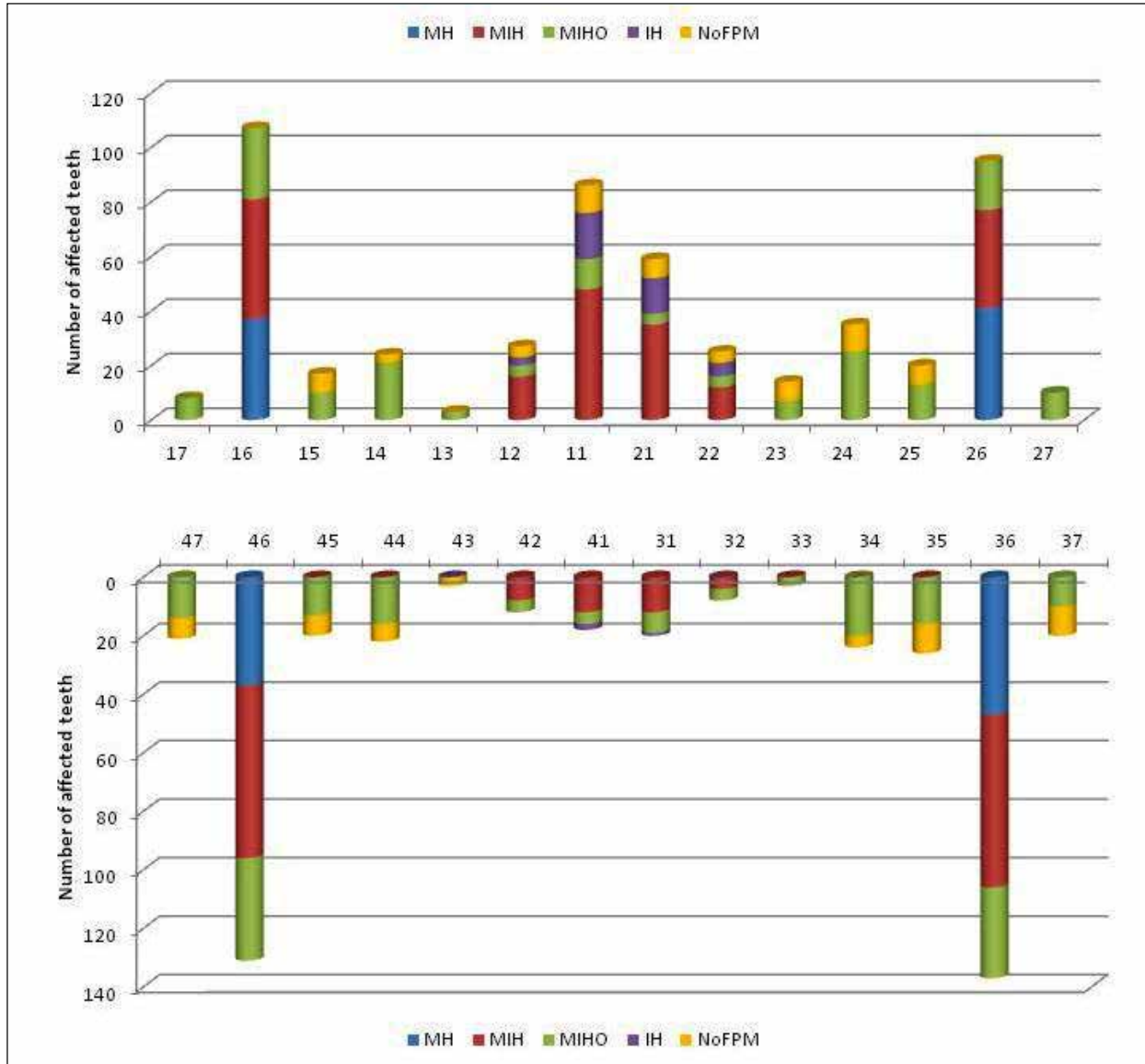
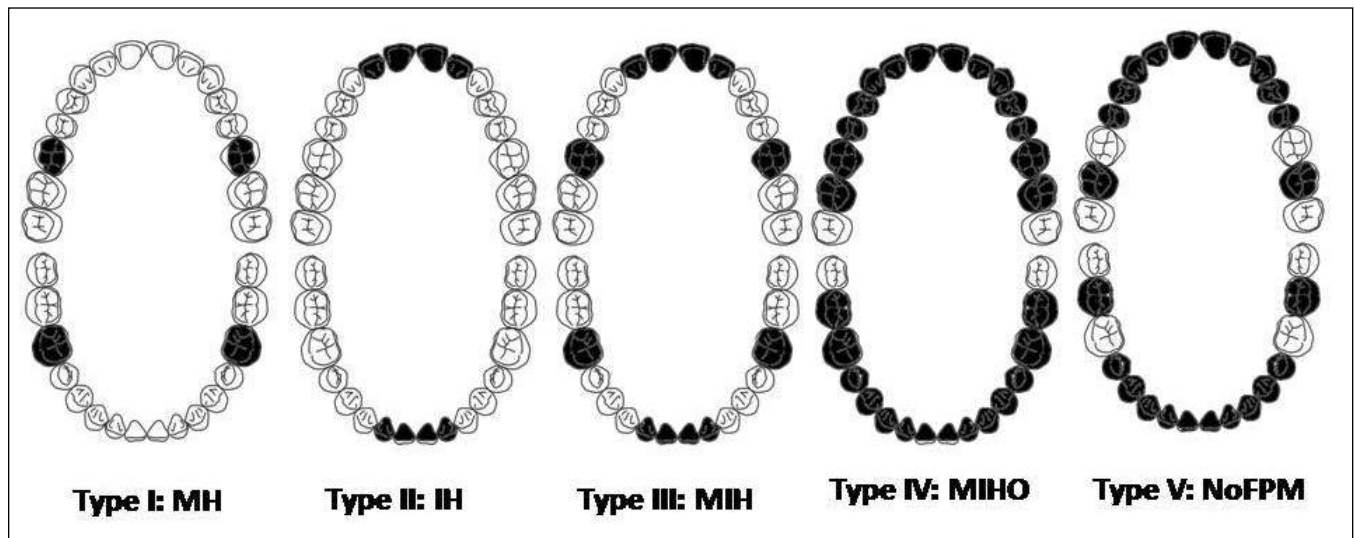


Figure 4: Classification of enamel hypomineralization (The shaded teeth represent the probable teeth which can be affected in any combination or numbers)



Although few studies have reported the prevalence and severity of enamel hypomineralization in primary molars;⁵⁻⁹ data on extent of enamel hypomineralization in full complement of primary dentition is not available. Thus, future studies should be conducted to report the prevalence of enamel hypomineralization in all teeth of primary dentition recruiting younger subjects i.e. <6 years of age. Furthermore, relationship amongst primary and permanent dentition enamel hypomineralization should also be explored by examining subjects with mixed dentition i.e. 8-10 year olds.

Proposal for a classification scheme for enamel hypomineralization

In light of the findings of the present study, we suggest the following classes of enamel hypomineralization in permanent dentition based on phenotypes (Figure 4):

1. Type I (MH): Enamel hypomineralization affecting only FPMs
2. Type II (IH): Enamel hypomineralization affecting only PIs
3. Type III (M+IH): Enamel hypomineralization with concomitant involvement of FPMs and PIs, but not any other tooth
4. Type IV (MIHO): Enamel hypomineralization affecting at least one of the canines/premolars or 2nd molars with concomitant involvement of at least one FPM. PIs may be affected simultaneously.
5. Type V (NoFPM): Enamel hypomineralization affecting at least one of the canines/premolars or 2nd molars but not FPMs. PIs may be affected simultaneously.

Since, so many variations have been reported in prevalence as well as clinical features of MIH across various population groups, we suggest that future studies should be carried out to report on global utility and validity of this classification scheme.

CONCLUSIONS

Prevalence of enamel hypomineralization was 13.21% (228/1726) and prevalence of MIH (FPM hypomineralization i.e. phenotypes MH, M+IH and MIHO) was 9.79% (169/1726) in study population. Five different phenotypes were identified which varied in extent as well as severity of enamel hypomineralization. Greatest severity was reported for phenotype MIHO and least severity was reported for phenotype IH. This is the first study to report on extent and severity of enamel hypomineralization in full complement of permanent dentition using the EAPD 2003 criteria. Future studies to report on extent and manifestations of various phenotypes in permanent dentition, mixed dentition and primary dentition should be carried out.

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