# Determination of the Dental Arch Form in the Primary Dentition Using a Polynomial Equation Model

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## ABSTRACT

**Purpose:** Many geometric forms and mathematical functions have been proposed as models of the dental arch; however, no such information seems to be available for the primary dentition. The purpose of this study was to develop a model for dental arch form in the primary dentition.
**Methods:** The participants were 92 children (47 boys, 45 girls) in primary dentition. Dental casts were used to measure dental arch dimensions with digital calipers. The arch form was classified as round, long, and short. The values of A and B in the polynomial function formula $Y=Ax^m+Bx^n$ were calculated so that the curve would pass through all teeth in the arch. Data were analyzed and compared with the independent t-test and multiple regression analysis.
**Results:** There was significant difference between boys and girls in dental arch widths ($P$=0.025) and depths at mandibular primary canines ($P$<0.001) but not significant at the maxillary primary canines ($P$>.05). The width and depth of the arches at the primary canines correlated significantly with the width and depth at the primary molars ($P$<0.001).
**Conclusions:** The sixth-order polynomial function $Y=Ax^6+Bx^2$ is a potentially accurate mathematical model of arch form for primary dentition. (J Dent Child 2012;79 (3):136-142)

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Knowledge of dental arch forms and dimensions is useful in managing transient malocclusion and in predicting future orthodontic problems as well as normal occlusal changes in the primary and mixed dentition. It is also useful to track the proper sequential exchange of permanent teeth and to determine optimal occlusion.[1,2] Growth of the supporting bones and post-eruption movement due to habits and unbalanced muscular pressures contribute to variations in dental arch size and shape.[3,4]

Research in human anatomy, physical morphology, and dentistry has investigated the size and shape of dental arches with qualitative and quantitative methods.[1] Although there are many studies about permanent dental arch morphology, accurate description of the morphology of primary dental arches is lacking. Moreover, the subjects of almost all studies of primary dental arch form to date are limited to certain geographical origins.[1,5-9] The data from these studies of form and size fail to provide relevant information regarding the population, as these people differ from western populations racially, culturally, and environmentally. An additional consideration is that racial difference in head form might be closely related to differences in arch dimension,[10] as suggested by the findings of racial differences in arch form type.[11-13]

Identifying appropriate arch form is key to achieve a stable, functional, and esthetic arch, and failure to customize arch form might lead to relapse and an unnatural smile.[14] In the past, the shape of the dental arch used to be describe in simple qualitative terms such as elliptic, parabolic, and U-shaped, or as segments of

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circles connected by straight lines. Such descriptions were obviously inadequate to precisely define it.[15] Linear measurements, such as arch width and depth, have also been used to describe arch shapes.[16-19] Many geometric forms and mathematical functions have been proposed as models of the human dental arch. Some studies presented a model function of mixed or permanent dentition, which can be considered a potentially accurate mathematical model of the dental arch.[1,9,15,17,19-22] No data on the applicability of this formula in the pediatric population seem to be available for the primary dentition.

The purpose of this study was to develop a model for dental arch form in the primary dentition. A further aim was to investigate the applicability of the polynomial function ($Y=Ax^6+Bx^2$) to the primary dentition.

## METHODS

### SAMPLE SELECTION

Patients who attended the pediatric dental clinic at the School of Dentistry of the Shiraz University of Medical Science in Shiraz, Iran, were invited to participate. In order to enroll in the study, children had to be between the ages of 4 and 5 years and had to have an acceptable dental arch, i.e., a full complement of primary teeth with acceptable overjet and overbite, no crowding, no crossbites, no tooth size discrepancy, and a clinically acceptable arch symmetry. The exclusion criteria were: history of orthodontic treatment, visually apparent interproximal caries, history of dental trauma, crown restorations, thumb-sucking past the age of 3 years, evidence of a craniofacial syndrome, and facial asymmetry. Occlusion and skeletal growth patterns were not taken into consideration in the study design.

The study was approved by the Human Ethics Review Committee of the School of Dentistry at Shiraz University. Informed consent was obtained from the subjects' parents. Alginate impressions of maxillary and mandibular dental arches were taken by a pediatric dentist and were poured immediately. The dental casts were used to measure various dental arch dimensions.

### MEASUREMENT OF DENTAL ARCH DIMENSIONS

Landmarks were marked on each cast in pencil to ensure proper location of the landmarks in all casts by the same examiner. Specific dental arch parameters were measured in millimeters directly from the casts with digital calipers (Digimatic caliper no. 500-652, Mitutoyo Corp, Tokyo, Japan) to within the nearest 0.01 mm and were read di-rectly from the calipers (Figures 1A and 1B). A line between the distal part of the incisive papilla and distal aspect of the raphe was considered the midline. The following dimensions were measured:

1. inter-canine width—from the tip of the cusps of the left and right canines; [17, 23]
2. inter-first molar width—from the tips of the mesiobuccal cusps of the left and right first molars;[23]
3. inter-second molar width—from the tips of the mesiobuccal cusps of the left and right second molars; [23]
4. canine depth—from the contact of the central incisors to a line connecting the canine cusp tips;[17, 23]
5. first molar depth—from the contact of the central incisors (through the midline) to a line connecting the mesiobuccal cusp tips of the first molar in the maxilla and from the contact of the central incisors to a line connecting the distobuccal cusp tips of the first molar in the mandible; and
6. second molar depth—from the contact of the central incisors to a line connecting the distobuccal cusp tips of the second molar.[17]

Means and standard deviations were calculated for each parameter. Mean values in boys and girls were compared using the independent t-test. The Pearson's correlations coefficient and multiple regression analysis were employed to study the relationship between widths and depths of the primary canine and molars in the maxillary and mandibular arches. A $P<0.05$ was considered statistically significant.

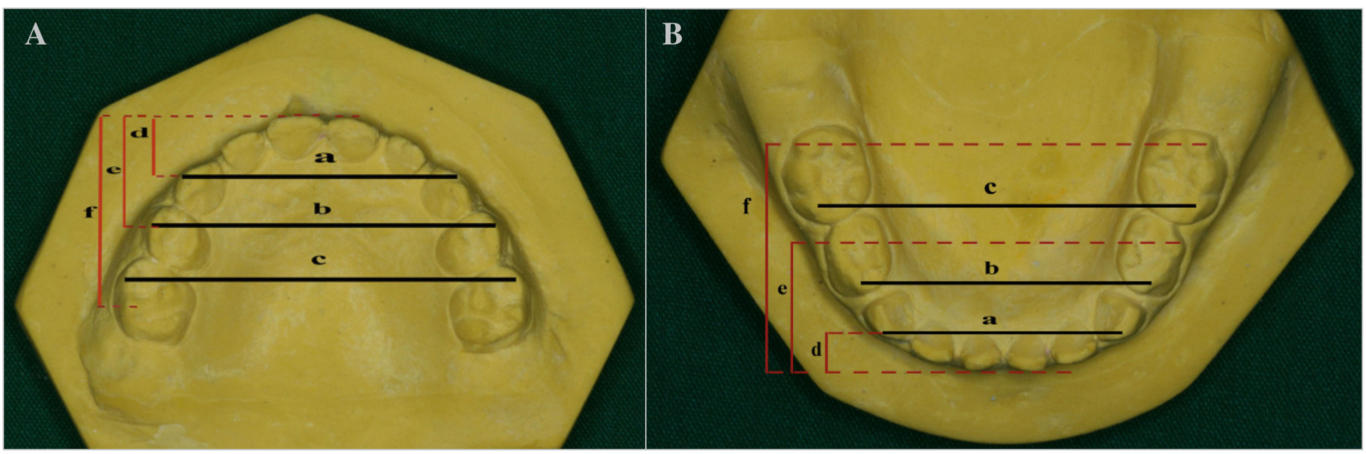


*Figure 1. (A) Measurement lines of maxillary and (B) mandibular dental arch width (continuous black line) and dental arch depth (dashed red line). Width: (a) inter-canine; (b) inter-first molar; (c) inter-second molar. Depth: (d) canine; (e) first molar; and (f) second molar.*

### EVALUATION OF DENTAL ARCH FORMS

Dental arch form in the primary dentition was assessed at the width and the depth of the second molars[9] and canines. Arch form was classified according to Tsai's criteria: round type (arch depth almost equal to half of the arch width), long type (arch depth longer than half of the arch width), and short type (arch depth shorter than half of the arch width).[9]

Mean depth and width were calculated for the maxillary and mandibular casts. A and B values in the sixth-order polynomial function $Y=Ax^6+Bx^2$ were calculated so that the curve of this formula would fit through the cusp tips of the canines and first and second molars. To verify that the formula was suitable for expressing the dental arch, the root mean square (**RMS**) errors between the original data and the fitted curve were calculated in each case. RMS is a standard mathematical tool to evaluate the similarity of 2 curves (the greater the similarity, the lower the RMS). For all the cases considered in the current study, the RMS error was less than 1 mm. A curve-fitting computer program was developed in a mathematical software (MATLAB 7.4.0) to calculate the values of A, B, and RMS for each of the casts. In constructing the curves, the investigators optimized the fit of the curve to the points while preserving widths and depths.

### RELIABILITY

To determine measurement error, 20 casts were selected at random and their measurements were repeated 25 days after the first measurement. The Pearson's correlation coefficient between the first and second measurements was high ($r=0.930$, $P<0.001$), and the difference between the first and second measurements was insignificant ($P=0.680$).

## RESULTS

Ninety-two children (47 boys, 45 girls), with a mean age 4.5 years, participated in the study. There were no significant differences between boys and girls in dental arch depths at the maxillary canines, first molars and second molars ($P>0.05$). The mean widths of the arch at the maxillary primary second molars was statistically significant between the genders ($P=0.014$). There also was a statistically significant difference between genders concerning the mean of dental arch width ($P=0.025$) and depth ($P<0.001$) at the mandibular canines and mandibular first molars ($P=0.008$). The mean values and standard deviations of dental arch widths and depths at the canines and molars are shown in Tables 1 and 2.

In both the maxilla and the mandible, there were significant correlations between width at the canines and the first molars (maxilla: $r=0.894$, $P<0.001$; mandible: $r=0.720$, $P<0.001$) and second molars (maxilla: $r=0.845$, $P<0.001$; mandible: $r=0.729$, $P<0.001$). Significant correlations were also seen between depth at the canines and the first molars (maxilla: $r=0.877$, $P<0.001$; mandible: $r=0.735$, $P<0.001$) and second molars (maxilla: $r=0.561$, $P<0.001$; mandible: $r=0.440$, $P<0.001$). Table 3 shows the regression models for the relationship between the width and depth at the canines and molars in both arches.

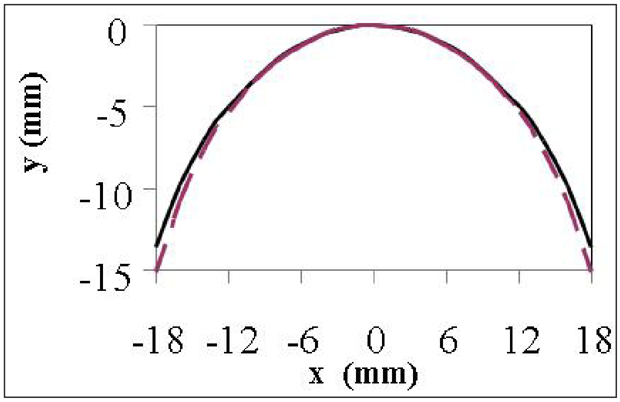


*Figure 2. Maxillary arch polynomial equations and superimposition of mean curves in boys (continuous line) and girls (dashed red line).*

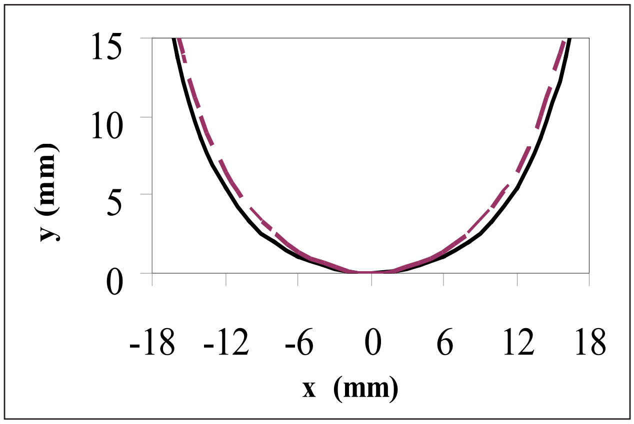


*Figure 3. Mandibular arch polynomial equations and superimposition of mean curves in boys (continuous line) and girls (dashed red line).*

At the second molars, almost all maxillary and mandibular dental arch forms were of the long type. At the maxillary canines, dental arches were almost all of the short type (98% in boys and 100% in girls). At the mandibular canines, dental arches were short in all participants (100%). There was no significant difference between genders in dental arch form at the canines and molars of both arches ($P>.05$).

To determine the function that best modeled the form of the primary dental arch, the data for boys and girls were pooled for further analysis. The sixth-order polynomial function $Y=Ax^6+Bx^2$, where x is the mean width and y is the mean depth, was found to be suitable for modeling the primary dental arches (Figures 2 and 3).

## DISCUSSION

This study found no significant differences between boys and girls in dental arch widths or depths at the maxillary canines. The results are consistent with the findings of Alhaija and Qudeimat,[7] who reported no significant differences between Jordanian preschool boys and girls in canine segment width.

In our study, width at the maxillary second molar was larger and widths of the mandibular canine and mandibular first molar were smaller in boys than in girls. Our analysis of possible sexual dimorphism also showed that boys had larger arch dimensions than girls.[1,5,7,8,20,24,25] Differences in measurement techniques and landmarks might account for the differences between our results and those of earlier studies in other populations. In this study, the second molar width was measured from the tips of its mesiobuccal cusps, according to Noroozi et al.[17] and Asakawa et al.[23] Prabhakaran et al.[2] however, measured interprimary molar width from the central fossa of the teeth.

In general, dental arches are roughly classified as square, ovoid, and tapered in prosthodontics, but these arch forms have not yet been mathematically defined. One solution may be to define them based on the relative ratios of the arch widths along with their relative depths.[17] The present study used these ratios and followed Tsai's method by classifying arches as round, long, or short types.[9] Because the shape of dental arches differs in the anterior and posterior seg-

***Table 1. Means and Standard Deviations of Dental Arch Width at the Canines and Molars in the Maxillary and Mandibular Arches by Gender (in mm)***

| | Maxilla | | | Mandible | | |
|---|---|---|---|---|---|---|
| Gender | Canines | First Molars | Second Molars | Canines | First Molars | Second Molars |
| Boys Mean±(SD) | 29.30±2.61 | 37.50±2.35 | 43.09±2.36 | 23.87±2.71 | 30.08±1.62 | 36.38±1.77 |
| Girls Mean±(SD) | 28.73±2.29 | 36.62±2.60 | 41.74±2.77 | 22.73±2.03 | 28.90±2.33 | 35.64±2.14 |
| Total Mean±(SD) | 29.02±2.46 | 37.07±2.50 | 42.43±2.64 | 23.26±2.43 | 29.45±2.10 | 35.98±2.00 |
| *P*-value | 0.270 | 0.092 | 0.014* | 0.025* | 0.008* | 0.074 |

***P<0.05.**

***Table 2. Means and Standard Deviations of Dental Arch Depth at the Canines and Molars in the Maxillary and Mandibular Arches by Gender (in mm)***

| | Maxilla | | | Mandible | | |
|---|---|---|---|---|---|---|
| Gender | Canines | First Molars | Second Molars | Canines | First Molars | Second Molars |
| Boys Mean±(SD) | 8.69±4.27 | 14.44±2.64 | 24.40±1.76 | 5.58±0.77 | 10.66±1.18 | 23.24±1.55 |
| Girls Mean±(SD) | 8.89±1.06 | 15.03±1.18 | 24.85±1.50 | 5.99±0.87 | 10.57±1.46 | 22.90±1.49 |
| Total Mean±(SD) | 8.79±3.13 | 14.73±2.07 | 24.62±1.64 | 5.80±0.85 | 10.61±1.33 | 23.06±1.52 |
| *P*-value | 0.761 | 0.170 | 0.193 | <0.001* | 0.745 | 0.287 |

***P<0.05.**

***Table 3. Regression Models for the Relationship between Width and Depth at the Canines and Molars in the Maxillary and Mandibular Arches****

| |
|---|
| **Maxilla** |
| Width of C=–2.136+1.167×(width of D)–0.285×(width of E) |
| Depth of C=–3.582+1.595×(depth of D)–0.452×(depth of E) |
| **Mandible** |
| Width of C=–9.926+0.369×(width of D)+0.620×(width of E) |
| Depth of C=–2.036+0.541×(depth of D)–0.086×(depth of E) |

****C= canine; D= first molar; E= second molar.***

ments,[1] the shapes of each segment were analyzed separately in this study. At the level of the second molar, the most frequent arch form in both arches was the long type, which agrees with Tsai.[9] Kook et al.[11] found that the most frequent arch forms were square in the Korean group and tapered in the white group. Nojima et al.,[26] found increased frequencies of ovoid and tapered arch forms and a decreased frequency of the square arch form in Caucasians, with a tendency to shift toward narrower forms in Caucasian compared to Japanese ethnic groups.

Population differences in body size, head form, and dentition are the result of genetic and environmental factors. Knowledge of these factors as sources of physical variation is important in determining the correct form and size for any given population.[27] Regardless of how strictly the samples are defined, our sample might not be representative of our populations. It should also be noted that linear measurements are, to some degree, inadequate for characterizing arch forms because they provide an incomplete description of all arch forms.[15]

Dental arch dimensions in the primary dentition determine, to a large extent, the alignment of teeth in the permanent dentition.[2] In this study, the mean inter-canine width was 29.02±2.46 mm in the maxilla and 23.26±2.43 mm in the mandible. This was different from the results reported by Prabhakaran et al.[2] Bishara et al.[28] reported a mean inter-canine width of 30.3 mm in the maxilla and 23.4 mm in the mandible. The present study found a mean inter-second molar width of 42.43±2.64 mm in the maxilla and 35.98±2.00 in the mandible. This was also different from the values reported by Bishara et al.,[28] who found a mean intermolar width of 43.5 mm in the maxilla and 36.9 mm in the mandible. However, it must be stated that their results were obtained from a different population and different age ranges.

The size and form of dental arches are generally defined by the positions of the teeth.[9] Changes in arch width involve growth of the alveolar process almost entirely, with little increase in skeletal width, especially in the mandibular arch.[2] There are clinically significant differences between the maxilla and mandible in regards to arch width, which correlate with different directions of vertical growth of the alveolar process in both arches. The maxillary alveolar processes diverge as the teeth erupt, whereas growth in the mandibular alveolar process is more parallel.[2] Different arch widths might be also attributed to the adaptability of the tongue to different arch depths, as reflected in the changes in lateral tongue size.[22]

This study showed that the sixth-order polynomial function $Y=Ax^6+Bx^2$, proposed by Noroozi et al.[17] for the permanent dentition,[17] is also an accurate mathematical model for primary dental arch forms. In this study, we used widths and depths at the canine and first and second molars. In contrast, Noroozi et al.[17] used widths and depths at the canines and second molars. Since the formula used in this study was based on a greater number of points and measurements, curve-fitting in this study might be assumed to be more accurate than in the report by them. It should be noted that the arch forms classified with this method were bilaterally symmetrical, even though mild asymmetry might occur naturally.[29] To reduce the effect of potential confounders on the results of this study, the number of factors considered was limited.[9]

In the current study, all participants had normal dental arch forms and no history of nonnutritive habits. Warren et al.,[30] concluded that long non-nutritive sucking habits influence dental arch form and occlusion as a result of increased overjet, open bite, and posterior crossbite. Factors such as posterior crossbite secondary to constricted maxilla may result in narrower maxillary arch width and may have a potential secondary effect on mandibular arch form.[30] It should also be noted that, in this study, the molar occlusal relation was not considered, and further studies are needed to determine the applicability of the polynomial function for different occlusal relations in the primary dentition.

Although trends in the dimensions of the dental arch were not considered in this study, it might be helpful to comment on the findings of some such studies. The relationship between dental arch dimensions and physical stature is known to be weak.[31] Although the average height and weight of children have increased over the past 50 years, this trend may not affect dental arch dimensions.[8] Approximately one half of the children nowadays are breastfed for at least part of their infancy.[32] Differences in infant feeding methods may affect the development of dental arches.[8,33] As craniofacial growth is influenced by the surrounding muscle force, difference in bite force, daily food intake, and lifestyle may be other factors that influence arch form.[34]

Further research is needed to establish effects of trends in the dimensions of dental arches and to follow dental arch dimensions from the primary to the mixed dentition period.

## CONCLUSIONS

Based on this study, the following conclusions can be made:

1. Dental arch width and depth at the primary canines correlated significantly with width and depth at the primary first and second molars.
2. The sixth-order polynomial function $Y=Ax^6+Bx^2$ was an accurate mathematical model of primary dental arch form.

Predicting changes in arch form and occlusion during the primary dentition can help establish acceptable esthetic and functional criteria for optimum occlusion at a later age.

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## REFERENCES

1. Tsai HH. Tooth position, arch size, and arch shape in the primary dentition. J Dent Child 2001;68: 17-22.
2. Prabhakaran S, Sriram CH, Muthu MS, Rao CR, Sivakumar N. Dental arch dimensions in primary dentition of children aged three to five years in Chennai and Hyderabad. Indian J Dent Res 2006; 17:185-9.
3. Verrastro AP, Stefani FM, Rodrigues CR, Wanderley MT. Occlusal and orofacial myofunctional evaluation in children with anterior open bite before and after removal of pacifier sucking habit. Int J Orthod Milwaukee 2007;18:19-25.
4. Vargervik K, Miller AJ, Chierici G, Harvold E, Tomer BS. Morphologic response to changes in neuro-muscular patterns experimentally induced by altered modes of respiration. Am J Orthod 1984;85: 115-24.
5. El-Nofely A, Sadek L, Soliman N. Spacing in the human deciduous dentition in relation to tooth size and dental arch size. Arch Oral Biol 1989;34: 437-41.
6. Janiszewska-Olszowska J, Stepien P, Syrynska M. Spacing in deciduous dentition of Polish children in relation to tooth size and dental arch dimensions. Arch Oral Biol 2009;54:397-402.
7. Abu Alhaija ES, Qudeimat MA. Occlusion and tooth/arch dimensions in the primary dentition of preschool Jordanian children. Int J Paediatr Dent 2003;13:230-9.
8. Warren JJ, Bishara SE. Comparison of dental arch measurements in the primary dentition between contemporary and historic samples. Am J Orthod Dentofacial Orthop 2001;119:211-5.
9. Tsai HH. Variations among the primary maxillary dental arch forms using a polynomial equation model. J Clin Pediatr Dent 2003;27:267-70.
10. Vela E, Taylor RW, Campbell PM, Buschang PH. Differences in craniofacial and dental characteristics of adolescent Mexican Americans and European Americans. Am J Orthod Dentofacial Orthop 2011; 140:839-47.
11. Kook YA, Nojima K, Moon HB, McLaughlin RP, Sinclair PM. Comparison of arch forms between Korean and North American white populations. Am J Orthod Dentofacial Orthop 2004;126:680-6.
12. Bayome M, Sameshima GT, Kim Y, Nojima K, Baek SH, Kook YA. Comparison of arch forms between Egyptian and North American white populations. Am J Orthod Dentofacial Orthop 2011: 139:e245-e252.
13. Gafni Y, Tzur-Gadassi L, Nojima K, McLaughlin RP, Abed Y, Redlich M. Comparison of arch forms between Israeli and North American white populations. Am J Orthod Dentofacial Orthop 2011:139:339-44.
14. McLaughlin RP, Bennet JC. Arch form considerations for stability and esthetics. Rev Esp Orthod 2000;29(3):216-33.
15. Al Harbi S, Alkofide EA, AlMadi A. Mathematical analyses of dental arch curvature in normal occlusion. Angle Orthod 2008;78:281-7.
16. Bonwill WGA. Geometric and mechanical laws of articulation: anatomical articulation. Transactions of the Odontological Society of Pennsylvania. Philadelphia: The Society; 1885:119.
17. Noroozi H, Hosseinzadeh Nik T, Saeeda R. The dental arch form revisited. Angle Orthod 2001; 71:386-9.
18. Germane N, Lindauer SJ, Rubenstein LK, Revere JH, Isaacson RJ. Increase in arch perimeter due to orthodontic expansion. Am J Orthod Dentofacial Orthop 1991;100:421-7.
19. Hnat WP, Braun S, Chinhara A, Legan HL. The relationship of arch length to alterations in dental arch width. Am J Orthod Dentofacial Orthop 2000;118:184-8.
20. Tsai HH. A computerized analysis of dental arch morphology in early permanent dentition. J Dent Child 2002;69:259-65.
21. Wellens H. Applicability of mathematical curve-fitting procedures to late mixed dentition patients with crowding: A clinical-experimental. Am J Orthod Dentofacial Orthop, 131:160.e17-160.e25, 2007.
22. Braun S, Hnat WP, Fender DE, Legan HL. The form of the human dental arch. Angle Orthod 1998; 68:29-36.
23. Asakawa A, Wakatsuki H, Asakawa T, et al. The characteristics of the deciduous dental arch form of children in Changchum City, Chin. Pediatr Dent J 2006;16:170-8.
24. Bishara SE, Khdivi P, Jackobson JR. Changes in tooth size arch length relationships from the deciduous to the permanent dentition: A longitudinal study. Am J Orthod Dentofacial Orthop 1995;108:607-13.
25. Ling JY, Wong RW. Dental arch widths of Southern Chinese. Angle Orthod 2009;79:54-63.
26. Nojima K, McLaughlin RP, Isshiki Y, Sinclair PM. A comparative study of Caucasian and Japanese mandibular clinical arch forms. Angle Orthod 2001;71:195-200.

27. Gupta R, Sivapathasundharam B, Einstein A. Eruption age of permanent mandibular first molars and central incisors in the south Indian population. Indian J Dent Res 2007;18:186-9.
28. Bishara SE, Jakobsen JR, Treder JE, Nowak A. Arch width changes from 6 weeks to 45 years of age. Am J Orthod Dentofacial Orthop 1997;111:401-9.
29. Kuswandari S, Nishino M. The mesiodistal crown diameters of primary dentition in Indonesian Javanese children. Arch Oral Biol 2004;49:217-22.
30. Warren JJ, Bishara SE, Steinbock KL, Yonezu T, Nowak AJ. Effects of oral habits' duration on dental characteristics in the primary dentition. J Am Dent Assoc 2001;132:1685-93.
31. Bishara SE, Jamison JE, Peterson LC, DeKock WH. Longitudinal changes in standing height and mandibular parameters between the ages of 8 and 17 years. Am J Orthod 1981;80:115-35.
32. Casiday RE, Wright CM, Panter-Brick C, Parkinson KN. Do early infant feeding patterns relate to breast-feeding continuation and weight gain? Data from a longitudinal cohort study. Eur J Clin Nutr 2004;58:1290-6.
33. Peres KG, Barros AJ, Peres MA, Victora CG. Effects of breastfeeding and sucking habits on malocclusion in a birth cohort study. Rev Saude Publica 2007; 41:343-50.
34. Katsaros C. Masticatory muscle function and transverse dentofacial growth. Swed Dent J Suppl 2001;151:1-47.