Dental arch dimensions in children with hypophosphataemic Vitamin D resistant rickets

*S.H. Al-Jundi *, Y.F. Al-Naimy*, S. Alsweedan***
**Dept. of Preventive Dentistry, **Dept. of Paediatrics, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan.*

Abstract:

AIM: This study evaluated dimensions of the dental arches of children affected with hypophosphataemic vitamin D resistant rickets (HVDRR), since no reports are available in the literature on the effect of this disease on the dental arches. **STUDY DESIGN:** comparative cross sectional. **METHODS:** The dimensions of the dental arches of 21 Jordanian children aged 3-16 years with HVDRR were measured and compared to those of matched healthy controls, using Paired t-test at the confidence level of 95%. One examiner performed all measurements on the models in a blind manner. **RESULTS:** Compared with healthy controls, a significant reduction in all transverse dimensions of the maxillary arch of diseased individuals was seen. Maxillary arch depth and arch perimeter were also significantly reduced in diseased individuals (P value 0.000 0.009, respectively). In the mandibular arch, a significant reduction was found in the inter-incisor, inter-canine and inter-first premolar widths in patients with HVDRR compared with normal controls (P values 0.005, 0.015 and 0.0035 respectively). Mandibular arch depth and arch perimeter were also significantly reduced. **CONCLUSIONS:** There is a trend towards smaller dental arches in patients with HVDRR compared with healthy controls. The results of the present study necessitate further exploration of the effect of this disease on dental arch development to improve dental management of this special need population.

Introduction

Four distinct forms of the inherited hypophosphataemic rickets had been reported, with three different modes of inheritance. X-linked Hypophosphataemia (XLH); is the most common heritable form of rickets in developed countries, accounting for 80% of HVDRR cases. The prevalence of X-linked hypophosphataemia (XLH), is about 1/20,000 live births [Jan and Levine, 2008], and is caused by inactivating mutations of the PHEX (Phosphate regulating gene with Homologies to Endopeptidases on the X-chromosome) gene [Filho et al., 2006]. The second form is Autosomal Dominant Hypophosphataemia (ADHR); which is a rare form of renal phosphate wasting; it is caused by mutation of FGF23 gene [Whyte and Thakke, 2005; L, U et al., 2006].

The third and fourth forms are inherited as Autosomal Recessive; both are rare forms of the disease, one is hypophosphataemia that is caused by mutations in dentine matrix protein 1(DMP1), the second form is hypophosphataemia with hypercalciuria (HHRH) and is caused by mutation in the NaPi-Iic [Negri, 2007].

Patients with HVDRR develop symptoms related to growth retardation and rachitic skeletal deformities including smooth bowing of the legs, gait disturbance, knock knees, metaphyseal widening, frontal bossing, and horizontal depression along the lower border of the chest [Farach-Carson and Nemere, 2003]. Laboratory Findings in these patients show hypophosphataemia with hyperphosphaturia, normocalcaemia with normal or reduced calciuria [Jan and Levine, 2008].

The defects in tooth mineralisation in patients with HVDRR have been extensively reported and include poorly mineralised, hypoplastic dentine, which consists of calcopherites rather than densely mineralized dentine [Seow, 1989]. These defects may extend to the pulp and facilitate the occurrence of dental abscesses often associated with this disease [Seow and Latham, 1986; McWhorter and Seale, 1991; Hillmann and Geurtsen, 1996]. Enamel hypoplasia [Goodman et al., 1998] and ectopically erupted permanent canines [Seow, 1995] have also been reported. Dental development in these patients was studied by Seow et al. [1995] who found no significant difference in dental age compared to chronological age in affected patients.

Regarding the craniofacial changes, craniosynostosis, and frontal bossing [Shetty and Meyer, 1991; Carlsen et al., 1984] have been reported. An old study in the literature reported retardation in the development of the mandible and maxillary length and depth [Tracy and Campbell, 1968].

Dental arches are part of the bony skeleton, bearing in mind that HVDRR is a condition that affects bone; little emphasis has been placed on the effect of this condition on the dimensions of the dental arches. A recent cephalometric study by Al-Jundi and co-workers [2009] found that patients with HVDRR have deficiency in the anterior cranial base length, maxillary length, and ramus height.

The dental arch dimensions of HVDRR patients have never been reported in the literature. Therefore the aim of this study was to investigate dental arch dimensions in patients with HVDRR, and to compare those dimensions with the values in healthy controls. This approach will provide baseline information on the effect of this disease on dental arch dimensions.

Key words: Arch dimensions, hypophosphatemic, Vitamin –D- resistant, rickets
Postal address: Dr S.H. S Al-Jundi. Po Box 810053. Irbid 22110. Jordan.
Email: aljundisuhad@yahoo.com

Materials and Methods

Study design. This was a comparative cross sectional study conducted in order to compare the values of arch dimension between patients with HVDRR and matched healthy controls.

Subjects. Permissions were obtained for the investigators to contact the physicians who treated the affected individuals to obtain access to their files. An informed consent was obtained from parents of all participants (affected and healthy). Infection control protocols were applied during both patients' examination and impression-making procedures.

The preliminary sample of 30 children diagnosed with HVDRR were recruited from Paediatrics, Nephrology and Orthopedic Departments in King Abdullah University Hospital in Irbid (Jordan) and Medical City of Royal Medical Services in Amman (Jordan). Patients' parents were contacted by telephone to explain the study aims, importance and related procedures and to get their consent for participation in the study. File records of affected patients were studied for medical history to ensure absence of any other systemic conditions and to check the diagnostic criteria, age of patient when starting treatment, medical treatment and the compliance regarding the provided treatment.

Exclusion criteria. For both the study and control groups, subjects were excluded if they had:

- Clinically evident approximal dental caries, restorations, or dental anomalies,
- Any oral habit that might influence the dental arches (e.g. digit sucking habits),
- Orthodontic treatment prior to the start of the examination,
- Any hereditary or acquired dental or facial deformity, syndromes and craniofacial conditions (e.g. Down's syndrome, cleft lip and palate),
- Control children should not have any moderate or severe skeletal malocclusion.

After examination applying the exclusion criteria, the sample consisted of 21 HVDRR patients whose age range was 3-16 years.

The control group was randomly selected from healthy Jordanian school children who did not fit the exclusion criteria, matched the affected individuals for age, sex, and teeth present. Accordingly each affected child had one healthy matching control.

Models. Upper and lower alginate (Tulip-CAVEX®) dental impressions were taken by one examiner (YFN). The impressions were cast in hard stone, after disinfection, on the same day in an attempt to reduce errors when producing the models. All dental arch measurement were made directly from the dental cast manually using a digital sliding caliper (Chenqdu tenggiang industry co. Ltd®) accurate to 0.05 mm by the same examiner (YFN. The measurements of the models were made in a blind manner after initial calibration of the examiner by an orthodontist to ensure compliance with measurements used and reproducibility. The reference points and landmarks used were similar to those in previous studies [Bishara et al., 1997, Bishara et al., 1998, Franchi et al., 2006] and included; the contact point between adjacent teeth, cusp tips of the canines, buccal cusps of first and second premolars and mesiobuccal cusps of the first permanent molars. In the case of primary molars the corresponding mesiobuccal cusps were used. In those instances where there was slight attrition, the landmark for that tooth was determined as the middle of the facet on the tooth. In subjects with an impacted maxillary canine, the interpremolar width was used to determine the anterior arch width instead of the inter-canine width as first premolar eruption precedes that of the permanent canine, its position in the arch is less affected by crowding [Al-Nimri and Gharaibeh, 2005].

Measurements. The following measurements were made:

- Arch width was measured as the distance from the cusp tip of one tooth to the cusp tip of the contralateral tooth, the inter-incisor width was measured from the distal contact point of the lateral incisor on one side to the distal contact point of the lateral incisor on the contralateral side [Bishara et al., 1997] (Fig 1).
- Arch depth was measured as the distance from the inter-incisal point to the mid distance of the inter-first permanent molar width [Franchi et al., 2006] (Fig 2).
- Arch length (perimeter) was measured as the sum of the segments between contact points from the mesiobuccal cusp of the first permanent molar to that of the opposite first permanent molar [Bishara et al., 1998, Franchi et al., 2006] (Fig 2).

Overjet and over bite were measured using the end of the digital calliper.

Statistical Analysis. For an error analysis 10 randomly selected casts were re-measured by the same examiner under the same conditions in order to calculate the coefficient of reliability for all the variables. The coefficient of the reliability was = 1-(Se2/St2), where the Se2 is the variance of the difference between the two replicates and St2 is the greater of the two variances of the two replicates. The results were used to estimate the random error using a coefficient of reliability by Houston [1983].

Figure 1. Transverse measurements (arch width); the inter-incisor (A1), inter-canine (A2), inter-first premolar (A3), inter-second premolar (A4), inter-first molar (A5).

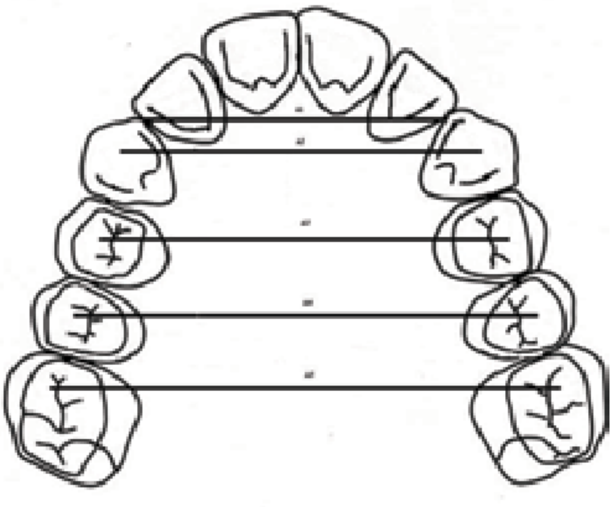
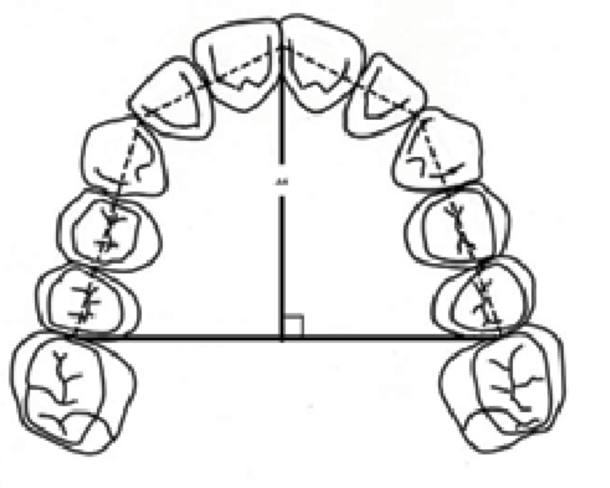


Figure 2: Arch perimeter (dotted line), and Arch depth (A6)



Statistical analysis was carried out using SPSS-V.12 program (statistical package for social sciences-Chicago, ILL). Summary statistics including mean, standard deviation (SD), and difference between means were calculated for each variable, test and control children were paired individually for the data comparisons, no pooling of values was performed due to the wide age range and small sample size. The one-sample Kolmogorov-Smirnov test was used to test the normality of distribution for both diseased and healthy variables. Paired t-test was used to evaluate difference between diseased and controls for the tested measurements. A statistically significant finding was considered present when P-values were below 0.05.

Results

Subjects. Of the 30 patients with HVDRR examined initially, only 21 fulfilled the inclusion criteria, the sample included 14 females and 7 males, their ages ranged from 3.4 to 16 years (mean age of 10.07±3.2), the control group ages ranged from 3 to 16.3 years.

The one-sample Kolmogorov-Smirnov test compares each variable with a specified theoretical normal distribution. This test resulted in that all the variables had no significant differences from the normally distributed model with P value ranging from 0.995 to 0.095. The results of the coefficient of reliability ranged from 0.95 for the mandibular inter premolar width to 0.98 for the maxillary inter-incisor width, and were considered acceptable for this study.

Model Measurements. The values of arch dimensions of the HVDRR patients and their controls are listed in Table 1. The results for the specific measurements were as follows:

Arch width: The maxillary arch width was significantly less in the affected group compared with healthy controls in all dimensions, P values were less than 0.03 (table 1). Whereas, in the mandibular arch, only the anterior arch width measurements (WL1, WL2 and WL3) were significantly reduced in the affected individuals in comparison to the healthy control group; with P values were less than 0.02.

Arch depth. The differences between the affected and healthy group in maxillary arch depth was on average 3.39 mm demonstrating a statistically significant reduction with P value 0.000. In the mandibular arch the affected group also had a statistically significant reduction in arch depth: P value 0.009.

Arch Perimeter: Both maxillary and mandibular arch perimeters were significantly smaller in the HVDRR group when compared with the normal individuals by an average of 5.46, 6.65 mm respectively with P value 0.009, 0.000.

Overjet, and overbite: Overjet was not significantly different in the diseased and controls. Overbite was reduced by 1.21 mm in the diseased individuals, however the difference was not significant.

Discussion:

Heredity, growth of bone, function, ethnic background, and inclination of the teeth are some of the factors that may affect the size and shape of the dental arches [Bjork et al., 1984; Hassanali and Odhiambo, 2000]. The effect of HVDRR on bone formed through the endocondral ossification is well studied. As this condition delays the process of bone formation and reduces the length of the bone it is not known whether this bone is affected and formed by means of intra-membranous ossification such as the dental arches. The results of this study may provide some information that can help determining the effect of HVDRR disease on arch dimensions.

Table 1: Mean values in mm, standard deviations, and statistical significances for the arch dimension measurements in HVDRR and healthy control Jordanian children.

			HVDRR patients		Control subjects				
Definition	**Variable**		**Mean***	**SD±**	**Mean***	**SD**	**Mean differences in pairs (mm)**	**Significance P value**	
Maxillary width									
Inter-incisor width	WU1		24.12	3.12	25.99	2.88	-1.88	*	0.028
Inter-canine width	WU2		29.47	1.88	32.2	2.2	-2.73	**	0.001
Inter-first premolar width	WU3		37.25	2.74	40.84	2.12	-3.59	**	0 .001
Inter-second premolar width	WU4		43.33	2.96	46.40	2.71	-3.07	**	0.004
Inter-first molar width	WU5		48.48	2.89	51.95	2.01	-3.47	**	0.006
Mandibular width									
Inter-incisor width	WL1		19.56	1.93	21.02	1.45	-1.46	**	0.005
Inter-canine width	WL2		24.71	2.18	26.45	1.49	-1.74	*	0.015
Inter-first premolar width	WL3		31.58	2.89	33.62	2.62	-2.05	*	0.0035
Inter-second premolar width	WL4		38.45	2.20	39.48	2.21	-1.03		0.121
Inter-first molar width	WL5		44.17	2.15	45.38	1.97	-1.21		0.211
Maxillary depth									
Arch depth	LU2		26.25	2.84	29.64	1.11	-3.39	***	0.000
Mandibular depth									
Arch depth	LL2		23.81	2.46	26.38	2.00	-2.57	**	0.009

In this study, the sample size was unavoidably small, due to the rarity of the condition on the one hand, and the limited accessibility to patients on the other hand. In Jordan, only patients with significant clinical manifestations are referred to two specialized medical institutes in order to provide treatment (Royal Medical Services and King Abdullah I Hospital). In addition, this study was interested in paediatric patients, which further reduced the sample size to 30 cases. From this sample, 9 cases were eliminated after applying the exclusion criteria.

This small sample size led to many drawbacks in the design of the study mainly the need to pool the ages and the sexes together. However pooling was done for the differences in the values between the affected and control groups not the values themselves and paired t-test was used rather than comparing the mean of the two populations. In that case pooling different age groups and sexes was not expected to affect the results, as the affected and control subjects were matched for age and sex.

In this study, it was found that the maxillary arch of patients with HVDRR was significantly smaller in length, depth, and width when compared with their healthy controls. A previous study of 9 children with Vitamin-D resistant rickets found that facial growth in these patients was retarded and that mandibular growth was less retarded than maxillary growth, which showed marked reduction in height and length using some cephalometric landmarks [Tracy and Cambell, 1968]. In a recent ceplalometric study of the craniofacial parameters in patients with HVDRR by Al-Jundi et al. [2009], it was found that these patients have a significant reduction of the maxillary length, SNA, ANB, and anterior caranial base length which may explain the findings of the current study. As the anterior cranial fossa is the template that establishes the basic dimensions of the maxilla [Enlow, 1983], the deficiency in the maxillary arch can be secondary to the deficiency in the anterior cranial base. It can also be due to the primary effect of the condition on membranous bone ossification. However, further longitudinal studies are required to establish the effect of this disease, and its treatment on development of the dental arches.

In the mandibular arch, a significant reduction in arch depth and arch perimeter compared with normal individuals was demonstrated. However, in the ceplalometric study of HVDRR patients, it was shown that the total mandiblulor length in these patients was not significantly changed; it also showed a reduction in the mandibular incisors' angle to the mandibular plane, and a reduced SNB angle [Al-Jundi et al., 2009]. This strongly indicates that the change in the above dimensions in the mandibular arch is due to retroclination of mandibular incisors rather than true deficiency in the arch itself.

In the mandibular transverse dimension, a reduction in the anterior arch width was noted which can also be due to alignment of the mandibular anterior teeth. The lower posterior arch width however, was not significantly reduced. This can be due to the tongue size effect that's highly correlated with the lower dental arch width especially in the posterior part [Tamari et al., 1991].

Conclusion

This study has laid down baseline data on arch dimensions of HVDRR patients to help establish effect of this disease on dental arches. Patients with HVDRR have a tendency towards smaller dental arches, especially the maxillary arch. Although the results of the present study showed several significant differences in arch dimensions between HVDRR group and control group, the small number of children studied allows only cautious interpretation of these results. Future longitudinal studies are required to establish the effect of HVDRR and its treatment on development of the dental arches.

Aknowledgements

The institutional review board (IRB) approval was obtained from the ethical committee of Faculty of Medicine in Jordan University of Science and Technology. We would like to acknowledge the contribution of Dr Issa Hazza from Royal medical Services, to the study sample collection. Also we would like to thank Dr Bader al deen Burgan for calibration of the examiner. We also would like to thank Jordan university of Science and technology for providing the grant for this study (no. 9/2008).

References

Al-Jundi SH, Dabouse IM, Al-Jamal GA. Craniofacial morphology in patients with Hypophosphatemic Vitamin-D-Resistant Rickets: A Cephalometric Study. J Oral Rehabil. 2009; 36:483-90.

Al-Nimri K. and Gharaibeh T. Space conditions and dental and occlusal features in patients with palatally impacted maxillary canines: an etiological study. Eur J Orthod. 2005; 16: 461-465

Bishara SE, Jakobsen JR, Treder J, Nowak A. Arch width changes from 6 weeks to 45 years of age, Am J orthod Dentofacial Orthop. 1997; 111: 401-409.

Bishara SE, Jakobsen JR, Treder J, Nowak A. Arch length changes from 6 weeks to 45 years of age. Angle Orthod. 1998; 68: 69-74.

Bjork A, Brown T, Skieller V. Comparison of craniofacial growth in Australian Aboriginal and Danes, illustrated by longitudinal cephalometric analysis. Eur J Orthod. 1984; 6:1–14.

Carlsen NLT, Krasilnikoff PA, Eiken M. Premature cranial synostosis in X-linked hypophosphatemic rickets: possible precipitation by 1 alpha-OH-cholecalciferol intoxication. Acta Paediatr Scand. 1984; 73: 149–154

Enlow DH. JCO/ Interviews Dr. Donald H. Enlow on Craniofacial Growth. J Clin Orthod. 1983; 17: 669 – 679.

Farach-Carson MC, Nemere I. Membrane receptors for vitamin D steroid hormones: potential new drug targets. Curr Drug Targets. 2003; 4: 67–76.

Filho HM, de Castro LC, Damiani D. Hypophosphatemic Rickets & Osteomalacia. Arq Bras Endocrinol Metab. 2006; 50: 802-813.

Franchi L, Baccetti T, Camporesi M, Lupolic M. Maxillary arch changes during levelling and aligning with fixed appliances and low-friction ligatures. Am J Orthod Dentofacial Othop. 2006; 130: 88-91.

Goodman JR, Gelbier MJ, Bennett JH, Winter GB. Dental problems associated with hypophosphataemic vitamin D resistant rickets. Int J Pediatr Dent. 1998; 8: 19–28.

Hassanali J, Odhiambo W. Analysis of dental casts of 6–8 and 12-year-old Kenyan children. Eur J Orthod. 2000; 22:135–142.

Hillmann G, Geurtsen W. Pathohistology of undercalcified primary teeth in vitamin D-resistant rickets: review and a report of two cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1996; 82: 218–24.

Houston WJ. Analysis of errors in orthodontic measurements. Am J Orthod Dentofacial Orthop. 1983; 83: 382-390

Jan SM, Levine MA. Perspective Molecular Pathogenesis of HypoPhosphatemic Rickets. Clinical Endocrinol Metabolism. 2008; 87: 2467–2473.

Liu S, Zhou J, Tang W, et al. Role of Fgf23 in Hyp mice. Am J Physiol Endocrinol Metab. 2006; 291: E38–E49.

McWhorter AG, Seale NS. Prevalence of dental abscess in a population with vitamin D-resistant rickets. Pediatr Dent. 1991; 13: 91-96.

Negri AL. Hereditary hypophosphatemias: New genes in the bone–kidney axis. Asian Pacific Soc Nephrology. 2007; 12: 317–320.

Seow WK, Latham SC. The spectrum of dental manifestations in vitamin D resistant rickets: implications for management. Pediatr Dent.1986; 8: 245–50.

Seow WK, Needleman HL, Holm IA. Effect of familial hypophosphatemic rickets on dental development: a controlled, longitudinal study. Pediatr Dent. 1995; 17: 346-350.

Seow WK, Romanink K, Sclavos S. Micromorphologic features of dentin in vitamin D-resistant rickets: correlation with clinical grading of severity. Pediatr Dent. 1989; 11:203–8.

Shetty NS, Meyer RA. Craniofacial abnormalities in mice with X-linked hypophosphatemic genes (Hyp or Gy). Tetralogy. 1991; 44: 463-72.

Tamari K, Shimizu K, Ichinose M, Nakata S, Takahama Y. Tongue volume and lower dental arch sizes. Am J Orthod Dentofac Orthop. 1991; 100: 453-458.

Tracy WE, Campbell RA. Dentofacial development in children with vitamin D-resistant rickets. J Amer Dent Assoc. 1968; 76: 1026-31.

Whyte MP, Thakke RV. Rickets and osteomalacia. The Medicine Publishing Company Ltd. 2005; 33: 70-74.