# Taurodontism and Van der Woude Syndrome

Is There an Association?

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## ABSTRACT

**Objective:** To report the occurrence of taurodontism in a clinical sample of Van der Woude syndrome (VWS) and describe its association with hypodontia and cleft type.

**Materials and Methods:** This retrospective, cross-sectional study was carried out on chart reviews and radiographs of 13 persons with VWS. Mean age was 10 years 11 months  $\pm$  1 year 5 months. Panoramic radiographs were used to confirm the presence or absence of teeth and to measure crown body and root lengths of mandibular first molars. Three-dimensional cone beam computed tomography (CT) scans were available on two persons with VWS. Both volumetric and linear measurements were obtained.

**Results:** The occurrence of taurodontism of the mandibular first molar was 35%: 27% hypodont and 8% mesodont. Of the 13 subjects with VWS, 6 (4 males and 2 females) had at least one tooth identified with taurodontism. Half of the cases were unilateral and half were bilateral, and all of the unilateral cases were on the left side. Five of the six subjects with taurodontism had missing incisors and premolars. Taurodontism was two times more frequent in those who were missing their second premolars than in those who had their second premolars. There was no correlation between cleft type and presence of taurodontism. The cone beam CT pilot study on two persons showed very abnormal morphology of both crown and roots, which was not apparent on the standard panoramic radiograph. Both the volumetric and linear measurements of the ratio of crown body to root were highly indicative of taurodontism. Further genetic studies are needed. **Conclusion:** There is a likely association between VWS and taurodontism.

KEY WORDS: Taurodontism; Van der Woude syndrome

# INTRODUCTION

Taurodontism is characterized by a large pulp chamber, and it is most commonly seen in molars. The term "taurodontism" was first used by Keith<sup>1</sup> to describe the teeth of prehistoric people, the Neanderthals and Heidelbergs. Taurodontism was a frequent finding in early humans and is most common today in Eskimos, possibly as a selective adaptation for cutting hide.  $^{\scriptscriptstyle 2}$ 

The genetic structure is likely polygenic (OMIM 272700). According to Shaw,<sup>3</sup> the trait is inherited as autosomal recessive. Autosomal dominant inheritance has been suggested by two-generation pedigree studies. However, Witkop<sup>4</sup> found no affected parents in the eight persons they investigated. Association of taurodontism with X-chromosome aneuploidy has been shown.5 According to some authors, taurodontism is most likely the result of disrupted developmental homeostasis.6 Late genes expressed during root formation (ALPL and DLX3) are associated with cementum agenesis (hypophosphatasia) and taurodontism. The epithelial- mesenchymal interactions governing root morphogenesis are poorly understood; therefore, little is known about how DLX3 mutations cause taurodontism.7

A taurodontic tooth is believed to result from a disturbance in Hertwig's epithelial root sheath. Based on this theory, there may be an association between tau-

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Accepted: October 2007. Submitted: August 2007. © 2008 by The EH Angle Education and Research Foundation, Inc.

rodontism and hypodontia as both conditions may have the same genetic etiology affecting the growth of dental epithelium.<sup>8</sup> The prevalence of taurodontism was reported to be 0.5% of Japanese,<sup>9</sup> 0.57–3.2% of white Americans,<sup>4.10</sup> 8% of Jordanian,<sup>11</sup> 33–41% of certain Africans,<sup>3</sup> and 46.4% of young adult Chinese.<sup>12</sup>

Taurodontism has been described together with congenitally missing teeth<sup>13–15</sup> and hypodontia in many syndromes,<sup>16</sup> in sex chromosome anomalies with extra X chromosomes,<sup>17,18</sup> and in persons with cleft lip and palate.<sup>19</sup> Other syndromes have also been reported to present with taurodontism: 18p11.3 deletion,<sup>20</sup> Smith-Magenis syndrome,<sup>21</sup> Tricho-dento-osseous syndrome,<sup>22–25</sup> Klinefelter's syndrome,<sup>26–28</sup> Williams syndrome,<sup>29</sup> McCune-Albright syndrome,<sup>30</sup> Down syndrome,<sup>31</sup> and Ellis-van Creveld syndrome.<sup>32</sup>

Van der Woude syndrome (VWS) is the most common cleft syndrome, occurring in approximately 2% of the population with facial clefts.<sup>33,34</sup> The prevalence of VWS varies from 1 in 100,000 to 1 in 40,000 stillborn or live births.<sup>35</sup> It is associated with lower lip pits (88%),<sup>36</sup> hypodontia (69%),<sup>37,38</sup> and cleft lip with or without cleft palate (21%).<sup>36</sup> A close association between VWS and congenital absence of second premolars has been shown.<sup>38–40</sup>

This disorder has an autosomal dominant inheritance pattern. The gene responsible in the vast majority of cases of this disorder, interferon regulatory factor 6 (IRF6), has been mapped to the long arm of chromosome 1 at q32-41.

The relationship between VWS and taurodontism has not been studied. The aim of this study is to report the occurrence of taurodontism in our clinical sample of VWS and to describe its association with hypodontia and cleft type.

#### MATERIALS AND METHODS

#### **Subjects**

This retrospective, cross-sectional study was carried using chart reviews and radiographs of 13 persons with VWS. Data gathered from the chart review included sex, age, and type of cleft. Subjects were identified from the University of California San Francisco Center for Craniofacial Anomalies computer database (Filemaker Pro 5.5, Apple Computers Inc, Santa Clara, CA, USA) using the key word "Van der Woude syndrome." All persons with VWS were included as the beginning sample frame. Twenty-five persons met our inclusion criteria of confirmed diagnosis of VWS, and clinical and radiographic records were available for review for 13 subjects (8 males, 5 females; 5 whites, 7 Hispanics, and 1 Pacific Islander). Mean age at the time radiographs were obtained was 10 years 11



**Figure 1.** Measurements of crown body and root length measured in millimeters on a mandibular first permanent molar as shown by Seow and Lai.<sup>14</sup>

months  $\pm$  1 year 5 months (range = 9 years 2 months to 13 years 11 months).

Panoramic radiographs were used to confirm the presence or absence of teeth and to measure crown body and root lengths of mandibular first molars using the method of Seow and Lai<sup>14</sup> (Figure 1). Periapical films were not available for review. All radiographs were obtained under the same conditions by the same technician and using the same machine. Although panoramic radiographs are not ideal for assessing taurodontism, Seow and Lai<sup>14</sup> have shown that a panoramic radiograph is equivalent to a long cone periapical radiograph for diagnosing taurodontism using their technique of measurement.

#### **Two-Dimensional Measurements**

The mandibular first permanent molar was selected for analysis as it is considered the most stable tooth of the series. This tooth was also selected because the entire outline of this tooth is clearly seen on the panoramic radiograph, in contrast to the maxillary molars where the root apices are usually obscured by the zygomatic bone; hence, root length is not easily determined. In addition, this is the only fully developed molar in the age group studied.<sup>14</sup>

The outlines of the mandibular first molars were transferred to an acetate tracing paper using a pencil (0.5 mm). A line representing the long axis of the tooth was then drawn from the deepest occlusal pit through the furcation area. Crown-body length was determined by measuring the distance from the deepest occlusal pit to the furcation area along the long axis. Root



Figure 2. Diagrammatic representation of the three classes of taurodontism as proposed by Shaw.<sup>3</sup>

length was determined from the furcation area to the most apical apex along the long axis. The molars were classified into three groups by ratio of crown body to root, indicating presence or absence of taurodontism (Figure2). The association of taurodontism with cleft type and number and location of missing teeth was assessed. One examiner performed all tracings and measurements twice with a two-week interval, and the measurements were statistically analyzed using Student's *t*-test for intrarater reliability.

#### **Three-Dimensional Measurements**

Three-dimensional (3-D) cone beam computed tomography (CT) scans were available on two subjects with VWS, one with taurodontism and one without according to the two-dimensional (2-D) measurements. The lower first molar was reoriented using software (On Demand 1.0.0.7059, CyberMed Inc, Seoul, Korea) such that the long axis of the tooth was perpendicular to the slices. Both volumetric and linear measurements were obtained. The DICOM (digital imaging and communications in medicine) data were imported into software (CB Works 2.01, CyberMed Inc, Seoul, Korea), and axial cross-sectional data were obtained for the mandibular left and right first molars. The area representing the tooth was segmented slice-by-slice using a threshold value higher than the surrounding bony structure. The segmented slices were stacked, providing a 3-D model of the tooth. The volume of the tooth was then measured. We calculated the volume of the crown body and root separately to obtain the ratio of crown body to root. Linear measurements were made from the slice at the level of the deepest pit of the crown to the level of furcation, and this was considered crown-body length. The linear measure from the slice at the level of furcation to the root apex was considered root length (Figure 3). We also obtained linear measurements of the ratio of crown body to root from the reconstructed tooth and compared the crown body to root ratios to the 2-D findings.



**Figure 3.** Sagittal slice of mandibular first molar showing linear measurements of CB and R length using CBworks (2.01).

## RESULTS

The 2-D inter-rater reliability showed no significant error based on Student's *t*-test. The occurrence of taurodontism of the mandibular first molar in the entire sample of left and right side molars was 9/26 or 35%: 27% hypodont and 8% mesodont (Table 1).

Six of the 13 subjects (4 males and 2 females) had at least one tooth identified with taurodontism. Half of the cases were unilateral and half were bilateral. All unilateral cases were on the left side. Five of the six subjects with taurodontism had missing incisors and premolars. Taurodontism was two times more frequent in those who were missing their second premolars. There was no correlation between cleft type and presence of taurodontism as shown by Fisher's exact probability test (Table 1).

3D Cone beam CT scans were available on two individuals with VMS, one with taurodontism and one without according to the 2D measurements. The 3-D volume of the right lower first molar in the subject with taurodontism was 1485.3 cc; crown volume was

 
 Table 1.
 Repeat Measurements of Crown Body to Root Ratios on Panoramic Radiographs Determining Presence and Degree of Taurodontism, Missing Teeth, and Cleft Type

		Right CB:R			Bight	Left CB:R			Left		
Gender	Age	1st	2nd	Mean	Diagnosis	1st	2nd	Mean	Diagnosis	Missing Teeth	CLP
Male	9 y, 3 m	1.1	1.1	1.1	Hypodont	1.1	1.1	1.1	Hypodont	4,7,10,13,20,29	CP
Male	10 y, 5 m	1.2	1.3	1.2	Hypodont	1.3	1.3	1.3	Mesodont	4,10,20,29	B-CLP
Male	11 y, 8 m	1.0	1.0	1.0	Normal	1.1	1.1	1.1	Hypodont	4,7,10,20,29	CP
Male	13 y, 11 m	1.0	1.0	1.0	Normal	1.4	1.6	1.5	Mesodont	4,7,10,13	B-CLP
Male	9 y, 2 m	1.0	1.0	1.0	Normal	0.8	0.8	0.8	Normal	29	CP
Male	9 y, 9 m	1.0	1.0	1.0	Normal	1.1	1.1	1.1	Normal	20	SMC
Male	10 y, 1 m	0.8	0.9	0.8	Normal	0.8	0.9	0.8	Normal		CP
Male	11 y, 0 m	1.0	0.9	0.9	Normal	0.9	0.8	0.9	Normal	7,10,23	B-CLP
Female	10 y, 9 m	1.2	1.2	1.2	Hypodont	1.2	1.3	1.2	Hypodont		SMC
Female	12 y, 0 m	0.8	0.9	0.9	Normal	1.1	1.1	1.1	Hypodont	7,8,9,10,20,29	B-CLP
Female	10 y, 4 m	0.9	0.9	0.9	Normal	0.9	1.0	0.9	Normal		CP
Female	11 y, 0 m	0.8	0.9	0.9	Normal	0.8	0.8	0.8	Normal	7,20,29	U-CLP
Female	13 y, 4 m	0.7	0.7	0.7	Normal	0.8	0.8	0.8	Normal	10	U-CLP

CB:R indicates crown body to root ratio; CLP, cleft lip and palate; CP, cleft palate; SMC, submucous cleft palate; B, bilateral; U, unilateral.

 Table 2.
 Linear Measurement of Crown Body and Root Lengths

 and Ratio on Reoriented Axial Views of Three-Dimensional Segmented Molars Determining Presence and Degree of Taurodontism

 and Comparison with Two-Dimensional Ratios<sup>a</sup> (R-Right, L-Left)

	Body (mm)	Root (mm)	3-D Ratio	Diagnosis	2-D Ratio	Diagnosis
Subject 1						
R	9.8	7.3	1.3	Mesodont	1.2	Hypodont
L	6.9	6.1	1.1	Hypodont	1.3	Mesodont
Subject 2						
R	7.5	8.2	0.9	Normal	0.9	Normal
L	8.9	7.9	1	Normal	0.8	Normal

<sup>a</sup> 3-D indicates three-dimensional; 2-D, two-dimensional.

1050.0 cc and root volume was 435.3 cc, giving a crown body to root ratio of 2.4. For the same tooth the 2-D crown body to root ratio was 1.3 (hypodont). We also measured the linear length of crown body and root from the reoriented axial slices and calculated the ratio, which was 1.33 (mesodont) (Table 2). For the left first molar the total volume was 2021.3, of which the crown volume was 1547.1, the root volume was 474.2, and the crown body to root ratio was 3.3; the 2-D ratio for the same tooth was 1.29 (hypodont). We also measured the linear length of crown body and root from the reoriented axial slices and calculated the ratio, which was 1.12 (hypodont) (Table 2).

The 3-D volume of the right lower first molar in the subject without taurodontism as assessed by 2-D measurements was 1209.6 cc, of which the crown volume was 849.2, the root volume was 360.5, and the crown body to root ratio was 2.4. For the same tooth, the 2-D ratio was 0.9 (normal). We also measured the linear length of crown body and root from the reoriented axial slices and calculated the ratio, which was 0.9 (normal) (Table 2).

For the left first molar the total volume was 1171.5, of which the crown volume was 859.2, the root volume was 312.3, and the crown body to root ratio was 2.8; the 2-D ratio for the same tooth was 0.8 (normal). We also measured the linear length of crown body and root from the reoriented axial slices and calculated the ratio, which was 1.0 (normal) (Table 2).

## DISCUSSION

To our knowledge, taurodontism has not been reported in VWS, although hypodontia is a frequent finding in this syndrome.<sup>38</sup> In our study, the prevalence of some degree of taurodontism in VWS was 6 of 13 subjects, almost 50%. In persons with VWS, the prevalence of hypodontia is significantly higher than in the cleft control population studied.<sup>38</sup> Therefore, the higher frequencies of hypodontia and taurodontism may have a common etiology. An association between taurodontism and hypodontia has been shown in Down syndrome.<sup>31</sup>

The association of taurodontism with hypodontia has been shown. Seow and Lai14 reported a taurodontism frequency of 35% in persons with hypodontia, and Schalk-van der Weide et al<sup>15</sup> found a frequency of 29% in those with oligodontia; however, only lower molars were assessed. Results of a study by Arte et al,8 confirmed findings of the association of taurodontism to hypodontia in previous studies. Their findings are in agreement with a Finnish study on cleft patients<sup>19</sup> showing the frequency of taurodontism to be 41% in 39 pairs of twins with cleft lip and/or palate and hypodontia. Their results indicate that malformed upper lateral incisors, rotation of premolars, and taurodontism are related to hypodontia and oligodontia. The same teeth are most often affected, and similar associated dental anomalies are also seen in syndromic



Figure 4. Three-dimensional volumetric rendering views of taurodont mandibular molar with six roots (CBworks 2.01) from (A) lingual (B) top and (C) bottom.

hypodontia. As genes play the main role in the etiology of congenitally missing teeth and several dental anomalies, it is recommended that a family history of hypodontia, oligodontia, and dental anomalies be noted in clinical assessments.

In the six subjexts with taurodontism, half were unilateral and half were on the left side. Previous studies<sup>41</sup> found bilateral prevalence of taurodontism in 1200 adult Israelis, whereas Seow and Lai<sup>14</sup> found that nearly half of their cases of taurodontism were unilateral with predominance for the left side. The severity of the cleft did not appear to correlate with occurrence of taurodontism.

The cone beam CT pilot study on two persons showed that the segmented teeth that were diagnosed with taurodontism on 2-D radiographs had very abnormal morphology of both crown and roots. One molar had six roots, three separate mesial and three distal; this was not apparent on the standard panoramic radiograph and to the best of our knowledge has not been reported previously (Figure 4). These malformations may common in VWS, but they have not been noted on standard radiographs.

The crown body to root ratio of the volume measurements indicated taurodontism in the subject who was found not to have taurodontism according to the 2-D radiographs. Volume measurements may not be useful in the diagnosing taurodontism but further studies are needed. The 3-D measurements of the crown body to root ratio were highly indicative of taurodontism in one subject, confirming the finding of taurodontism.

The clinical implication of taurodontism is a poten-

tially increased risk of pulp exposure because of decay and dental procedures. Taurodontism in combination with hypodontia may complicate orthodontic and/or prosthodontic treatment planning.

## CONCLUSION

- This study supports the concept that some common genetic mechanism may be responsible for VWS, hypodontia, and taurodontism.
- We have shown that the 3-D visualization of the molar using cone beam CT reveals more information. We have also shown a new method to assess taurodontism with a true representation of the crown body to root ratio.

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