H Lauridsen
BF Hansen
I Reintoft
JW Keeling
LT Skovgaard
I Kjær

Short hard palate in prenatal trisomy 21

Authors' affiliations:
Halfdan Lauridsen, Birgit Fischer Hansen, Department of Pathology, Hvidovre University Hospital, Copenhagen, Denmark
Ingermarie Reintoft, Department of Pathology, Central Hospital, Esbjerg, Denmark
Jean W. Keeling, Department of Pediatric Pathology, The Royal Hospital for Sick Children, Edinburgh, UK
Lene Theil Skovgaard, Department of Biostatistics, Department of Public Health, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark
Inger Kjær, Department of Orthodontics, School of Dentistry, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark

Correspondence to:
Inger Kjær
Department of Orthodontics
School of Dentistry
Faculty of Health Sciences
University of Copenhagen
Nørre Alle 20
DK-2200 Copenhagen N
Denmark
Tel.: +45 35 32 66 70
Fax: +45 35 32 66 86
E-mail: ik@odont.ku.dk

Dates:
Accepted 27 February 2005

To cite this article:
Orthod Craniofacial Res **8**, 2005; 91–95
Lauridsen H, Hansen BF, Reintoft I, Keeling JW, Skovgaard LT, Kjær I:
Short hard palate in prenatal trisomy 21

Structured Abstract

Authors – Lauridsen H, Hansen BF, Reintoft I, Keeling JW, Skovgaard LT, Kjær I

Objective – The aim of the present study was for the first time to examine on postmortal material the total midpalatal length of the hard palate and the length of its two components (the maxillary and palatine parts) in trisomy 21 fetuses, and to compare the results to normal standards.

Design – Material from 31 human fetuses with genetically verified trisomy 21 was studied. The fetuses were derived from legally induced or spontaneous abortions. Palates were, after sectioning, radiographed in lateral projection (Grenz Ray radiographic apparatus). Cephalometric measurements were performed with a digital caliper. Statistically, the length measurements for the two groups were compared, adjusting for crown rump length (CRL) through linear regression. At two specific ages (150 and 170 mm CRL), the length of the palatal components in trisomy 21 was compared to normal standards.

Results – For CRL 150 mm and CRL 170 mm it appears that all three palatal lengths, total length, maxillary length, and palatinal length are significantly shorter in fetuses with trisomy 21.

Conclusion – The main conclusion of our study is that the total palatal length in prenatal trisomy 21 is shorter than normal and that this is due both to a shortness of the maxillary and the palatine components of the hard palate.

Key words: bone; development; genotype; maxilla; palatina; phenotype; radiology

Introduction

From postnatal radiographic investigations of trisomy 21 subjects, it is known that the palate from birth is shorter than in the normal genotype. This was shown by Kisling (1) and confirmed by Westerman *et al.* (2) and Fischer-Brandies (3).

Recently, Cicero *et al.* (4) have documented by ultrasound investigations that the maxillary length was significantly shorter in human fetuses with trisomy 21 in the age range of 11–14 weeks of gestation compared with normal fetuses.

The hard palate is composed of horizontal processes from the maxillary bone and horizontal processes from the palatal bone. In only one study on prenatal palatal development in trisomy 21 fetuses distinction is made between development of these different components (5). This histological investigation showed that there are different types of malformations in the horizontal part of the palatine bone in human trisomy 21 fetuses.

In the scientific literature on prenatal bone development in trisomy 21 it is shown that there are many osseous components that are smaller or shorter in trisomy 21 compared to normal conditions. Thus, FitzSimmons *et al.* (6) described short longbones in trisomy 21. Later examples are: short iliac bone (7); short bones in the third finger (8); short femura, tibea, nasal bone, and middle phalanx of the fifth digit (9); short femur length (10); short nasal bone (11); and short humerus (12). These investigations are partly postmortal and partly ultrasonographic.

Concerning the normal prenatal palate, standards exist on length measurements of the palate evaluated postmortally. Standards exist concerning the length of the maxillary and of the palatal components and of the total hard palate (13).

The aim of the present study was to examine on postmortal material the total midpalatal length of the hard palate and the length of its two components (the maxillary and palatine parts) in trisomy 21 radiographically, and to compare these measures to the normal development.

Materials and methods

Material from 31 human fetuses with genetically verified trisomy 21 was included in this study. The fetuses were derived from legally induced or spontaneous abortions examined at the Department of Pathology, Hvidovre University Hospital, Denmark; at the Department of Pathology, Central Hospital, Esbjerg, Denmark; and at the Department of Pediatric Pathology, the Royal Hospital for Sick Children, Edinburgh, UK. All material was investigated as part of required autopsies in compliance with the regulations concerning parental consent.

Twenty of the fetuses investigated are identical to the ones included in the histological study of the palatine bone by Lauridsen *et al.* (5).

Crown rump length (CRL) of the fetuses ranged from 120 to 215 mm, corresponding to 16–25 weeks of gestational age.

Palates from the 31 fetuses were radiographed after sectioning in lateral projection according to a method described by Kjær (14). The Grenz Ray radiographic apparatus used was a Hewlett Packard Faxitron unit (model 43805/N; McMinnvill, Tennessee, OR, USA), the tube voltage varying from 15 to 40 kV, and the exposure time from 10 to 30 s at 2.5–3.0 mA. Kodak X-Omat film was used, routinely processed.

Cephalometric measurements were made between reference points, as shown in Fig. 1 and listed in Table 1, according to the method described by Silau *et al.* (13). Only when the reference points were clearly visible the measurements were obtained. Thus, the total length of the palate (T), from the anterior nasal spine to the posterior part of the maxillary component could be measured in 30 fetuses. The length of the palatine component (P), from the anterior part of the palatal bone to the posterior nasal spine, was measured in nine fetuses, whereas, the maxillary component (M) could be measured in 31 cases. The measurements were recorded with a digital caliper (Jocal; C.E. Johansson AB, Eskilstuna, Sweden).

The relation between the components of the palatal length and fetus age (through the proxy CRL) was investigated using linear regression. The slopes for the two groups, the trisomy 21 group and the normal group (13), were compared, as were the palatal lengths at CRL 150 and 170 mm.

Results

Estimated regressions lines for the two groups are presented in Fig. 2. Comparisons of the slopes appear in Table 2, which shows that for the maxilla, the growth is significantly slower in prenatal trisomy 21 compared to normal. The same tendency is seen for the total length, although the difference is not significant here. For the palatine component, the sample size is too

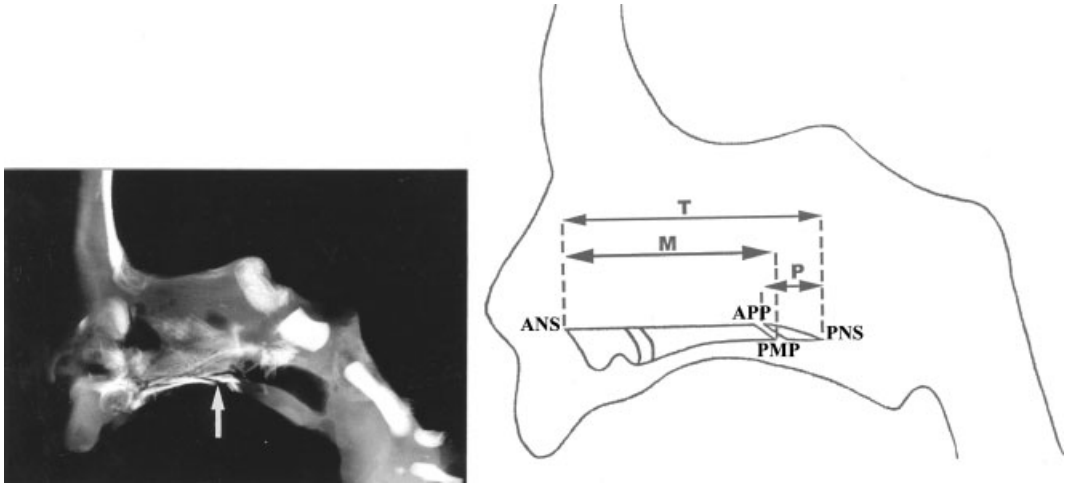

Fig. 1. Left: Radiograph of the midsagittal tissue block from a human fetus with trisomy 21. CRL = 171 mm. The arrow marks the location of the transpalatinal suture. Anterior to the arrow (left) is the maxillary part of the hard palate. Posterior to the arrow (right) is the palatal part of the hard palate. Right: Drawing of the palatal contour from a human fetus as shown to the left. T, total palatal length from the reference points ANS to PNS; M, maxillary length from the reference points ANS to PMP; P, palatal length from the reference points APP to PNS.

Table 1. **Reference points**

ANS	Spinal point	Apex of the anterior nasal spine
PMP	Posterior maxillary point	Most posterior point of the maxillary component
APP	Anterior palatine point	Most anterior point of the palatine bone
PNS	Posterior spinal point	Apex of the posterior nasal spine

small to make a meaningful comparison. For CRL 150 mm and CRL 170 mm it appears that all three palatal lengths, total length (T), maxillary length (M), and palatinal length (P) are significantly shorter in fetuses with trisomy 21 (Table 3).

Discussion

The main conclusion of our study is that the total palatal length in prenatal trisomy 21 is shorter than normal and that this is due both to a shortness of the maxillary and to the palatine components of the hard palate. The finding of a short palate corresponds well to the postnatal descriptions of the hard palate as being smaller than normal (1–3). In postnatal life it is not possible to distinguish the maxillary and the palatine components radiographically. Thus, for the first time it is shown in this study that both components of the hard palate are short in trisomy 21.

In a recent study on maxillary length at 11–14 weeks of gestation, the designation 'maxillary' must be synonymous with 'palatal'. Furthermore, 11 weeks of gestation is very early to be able to measure palatal length, as this is when the palate develops from the soft tissue palatal shelves and before ossification starts (14).

The purpose of assessing palatal lengths focusing on fetuses from 150 mm CRL is that from this age the palates are fully developed in the osseous structure. The cleft malformations identified in prenatal trisomy 21 in our previous histological study partly on the same material (5) could not be identified on the radiographs due to superposing of anatomical structures.

Postnatally, it has been described that trisomy 21 patients have a short stature but normal weight (15).

A fundamental problem in relating prenatal palatal length to a fetal size parameter, as performed in this study, is that the fetal length (CRL) in relation to gestational age may be shorter in trisomy 21 than in normal fetuses. We have not taken this aspect into account. However, if a trisomy 21 fetus of 150 mm CRL is older than a genotypically normal fetus of 150 mm CRL and therefore ought to be compared to normal fetuses larger than 150 mm CRL, then the difference between actual bone sizes would be even more significant than shown in this study.

The purpose of diagnosing bone sizes in prenatal trisomy 21 is to present a tool that could be used ultrasonographically for diagnostics. Ultrasonographic marker for trisomy 21 is nuchal thickness in the first or

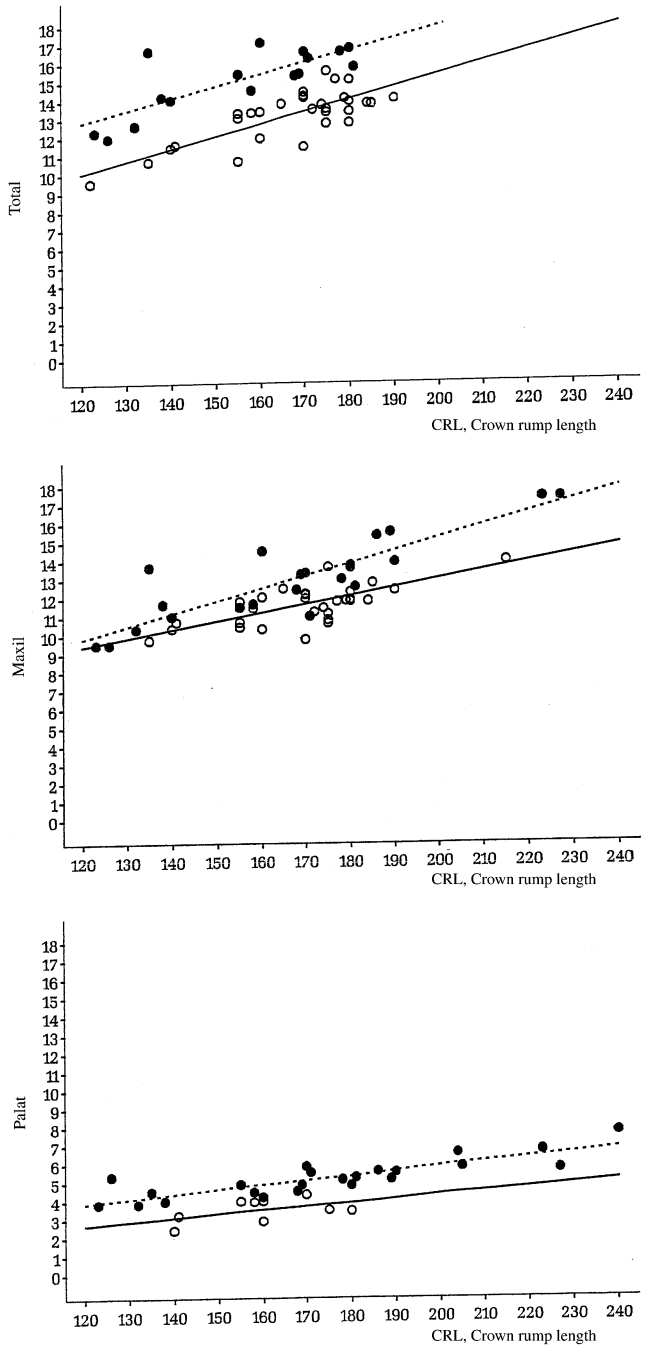

Fig. 2. Total prenatal palatal length and length of hard palate components (maxillary part and palatal part) in mm. Upper: Total palatal length (Total) in prenatal trisomy 21 (solid line) related to CRL. Normal total palatal length is marked with broken line.
Middle: Maxillary length (Maxil) in prenatal trisomy 21 (solid line) related to CRL. Normal values are marked with broken line.
Lower: Length of the palatal component of the hard palate (Palat) in prenatal trisomy 21 (solid line) related to CRL. Normal values are marked with broken line.

second trimester related to the length of specific bone components as for instance the length of the nasal bone. Graupe *et al.* (16) have described nuchal thickness as the most useful marker for trisomy 21.

Table 2. **Comparison of slopes (trisomy 21 vs. normal)**

Length	*T*-test	*p*-value	Estimated difference (with confidence interval)
Maxilla	−2.48	0.017	−0.0367 (−0.0664, −0.0070)
Palatal	−0.28	0.78	−0.0041 (−0.0337, −0.0256)
Total	−1.14	0.17	−0.0183 (−0.0443, −0.0078)

Table 3. **Estimated difference (trisomy 21 vs. normal) with confidence interval and included *p*-values**

Length	CRL = 150		CRL = 170	
	Difference	*p*-value	Difference	*p*-value
Maxilla	−1.129 (−2.011, −0.247)	0.013	−1.863 (−2.482, −1.243)	<0.0001
Palatal	−1.305 (−1.857, −0.752)	<0.0001	−1.386 (−1.913, −0.859)	<0.0001
Total	−2.789 (−3.513, −2.065)	<0.0001	−3.154 (−3.704, −2.604)	<0.0001

The present study is a postmortem study and only the results concerning total palatal length may prove to be useful in ultrasonographical diagnostics. The work, though, may be important in order to understand early phenotypical deviations in genotypic disorders. Furthermore, the knowledge that the short palate is a result both of short maxillary horizontal bony processes and short palatinal horizontal bony processes is valuable for the understanding of the postnatal development of a short palate in trisomy 21.

References

1. Kisling E. *Cranial morphology in Down's syndrome.* Copenhagen: Munksgaard; 1966.
2. Westerman G, Johnson R, Cohen M. Variation of palatal dimensions in patients with Down syndrome. *J Dent Res* 1975;**54**:767–71.
3. Fischer-Brandies H. *Entwicklungmerkmale des Schädels und der Kiefer bei Morbus Down unter Berücksichtigung der funktionellen kieferorthopädischen Frühbehandlung.* Berlin: Quintessenz Verlags-BmbH; 1988.
4. Cicero S, Curcio P, Rembouskos G, Sonek J, Nicolaides KH. Maxillary length at 11–14 weeks of gestation in fetuses with trisomy 21. *Ultrasound Obstet Gynecol* 2004;**24**:19–22.
5. Lauridsen H, Fischer HB, Reintoft I, Keeling JW, Kjaer I. Histological investigation of the palatine bone in prenatal trisomy 21. *Cleft Palate Craniofac J* 2001;**38**:492–97.
6. FitzSimmons J, Droste S, Shepard T, Pascoe-Mason J, Chinn A, Mack L. Longbone growth in fetuses with Down syndrome. *Am J Obstet Gynecol* 1989;**161**:1147–77.

7. Zoppi MA, Ibba RM, Floris M, Monni G. Can fetal iliac bone measurement be used as a marker for Down's syndrome screening? *Ultrasound Obstet Gynecol* 1998;**12**:19–22.
8. Kjaer MS, Keeling JW, Andersen E, Fischer HB, Kjaer I. Hand development in trisomy 21. *Am J Med Genet* 1998;**79**:337–42.
9. Stempfle N, Huten Y, Fredouille C, Brisse H, Nessmann C. Skeletal abnormalities in fetuses with Down's syndrome: a radiographic post-mortem study. *Pediatr Radiol* 1999;**29**:682–88.
10. Snijders RJ, Platt LD, Greene N, Carlson D, Krakow D, Gregory K, et al. Femur length and trisomy 21: impact of gestational age on screening efficiency. *Ultrasound Obstet Gynecol* 2000;**16**: 142–5.
11. Tuxen A, Keeling JW, Reintoft I, Fischer HB, Nolting D, Kjaer I. A histological and radiological investigation of the nasal bone in fetuses with Down syndrome. *Ultrasound Obstet Gynecol* 2003;**22**:22–6.
12. Longo D, DeFigueiredo D, Cicero S, Sacchini C, Nicolaides KH. Femur and humerus length in trisomy 21 fetuses at 11–14 weeks of gestation. *Ultrasound Obstet Gynecol* 2004;**23**:143–7.
13. Silau AM, Njio B, Solow B, Kjaer I. Prenatal sagittal growth of the osseous components of the human palate. *J Craniofac Genet Dev Biol* 1994;**14**:252–6.
14. Kjær I. Prenatal skeletal maturation of the human maxilla. *J Craniofac Genet Dev Biol* 1989;**9**:257–64.
15. Toledo C, Alembik Y, Aguirre JA, Stoll C. Growth curves of children with Down syndrome. *Ann Genet* 1999;**42**:81–90.
16. Graupe MH, Naylor CS, Greene NH, Carlson DE, Platt L. Trisomy 21. Second-trimester ultrasound. *Clin Perinatol* 2001;**28**:303–19.