Original Article

Cranial base, maxillary and mandibular morphology in Down syndrome

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ABSTRACT

Objective: To test the null hypothesis that there is no difference between craniofacial measurements of individuals with Down syndrome (DS) and normal controls.

Materials and Methods: A cephalometric analysis including additional landmarks and measurements to study specific craniofacial features was undertaken on pretreatment cephalograms of 25 patients with DS (12 male, 13 female; mean age 15.1 years) treated at The Hospital for Sick Children, Toronto. Measurements were compared with those from cephalograms of racial groups age and gender matched, normal, Class I children, available from the Burlington Growth Center. Data were analyzed using paired *t*-tests.

Results: Large reductions were measured in the size and spatial relationships of craniofacial structures in the DS group. The greatest differences included a larger cranial base angle; reduced elevation of sella from FHP; reduced anterior and posterior cranial base lengths; reduced anterior and posterior face heights; smaller maxilla with reduced anterior basal and apical dimensions; and smaller mandibular ramus, body and symphyseal dimensions and proclined symphysis. Maxillary incisors were severely proclined and undererupted, while mandibular incisors were undererupted. Alveolar heights were reduced. Anterior open bite was frequently noted. Maxillary and mandibular planes exhibited forward rotation patterns, promoting overclosure. Mandibular hypoplasia was less severe than cranial base and maxillary hypoplasia. Hypodontia of one or more permanent teeth was found in 92% of the sample.

Conclusions: The null hypothesis was rejected. Significant hypoplasia in endochondral, mesodermal, and ectomesenchymal derived structures of the cranium and face in subjects with DS was clearly evident. More severe platybasia than previously reported was found. (*Angle Orthod.* 2010;80:861–869.)

KEY WORDS: Down syndrome; Cephalometrics; Craniofacial; Cranial base; Maxilla; Mandible

INTRODUCTION

Down syndrome (DS), also known as trisomy 21, is the most well-known chromosomal disorder, characterized by generalized growth and mental deficiency and affects 1 in 600 to 1 in 2000 live births.[1] It is an easily recognized, congenital autosomal disorder in which there is an extra chromosome 21, translocation, mosaicism, or partial trisomy. Apparently, there is no racial, socioeconomic, or gender predilection, but increasing maternal age is associated with increased prevalence. The syndrome is named after John Langdon Down, who in 1866 accurately described many of its characteristics.[2]

With its characteristic facies of a small cranium, midface and nasal bone depression, flat malar processes, upward slanting eyes, and strabismus, this syndrome is easily recognized. A number of previous reports have aimed to describe the craniofacial features in Down syndrome.[3–9] Reduced maxillary length and midface retrusion have been historically reported in the literature.[4,7,8,10,11] The cranial base is small[3–13] and the cranial base angle is increased.[3,7,8,12] However, many aspects of the craniofacial morphology remain unclear. Some authors have described the

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Table 1. Sample Characteristics

Age in Years												
Down Syndrome Group (N = 25)						Control Group (N = 25)					
Mean	SD	Range				Mean	SD	Range			
15.0	1.9	11.5–18.3				15.1	2.4	12.0–18.1			
Male (N = 12)			Female (N = 13)			Male (N = 12)			Female (N = 13)		
Mean	SD	Range	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range
14.9	1.9	12.5–18.3	15.1	1.9	11.5–18.0	15.1	1.6	13.0–18.1	15.1	2.0	12.0–18.1

mandible as small,[6,14] while others have found it to be similar to the unaffected population.[8,9] Detailed morphologic features of the jaws including the dimensions and relations of the mandible (specifically the body, ramus, and chin), the anterior maxilla, and the alveolar dimensions have not been well described. In fact, a relatively recent cephalometric report described both the maxilla and mandible to be similar to published mesofacial norms for similar ages.[9] We aimed to test the null hypothesis that there is no difference between the craniofacial measurements of individuals with Down syndrome and normal controls through a comprehensive cephalometric analysis.

MATERIALS AND METHODS

This retrospective cephalometric and radiographic study was conducted using the pretreatment cephalometric and panoramic radiographs of patients with Down syndrome who had received or are receiving orthodontic treatment in the orthodontic clinic at The Hospital for Sick Children, Toronto, Canada. The radiographs used in this study had been acquired as part of these patients' diagnostic records for clinical decision making or for following treatment progress and were available in the cephalometric archives of the hospital's craniofacial center. The hospital's research ethics board approved the research protocol.

Preorthodontic treatment radiographic and clinical records of 25 subjects with DS (12 male, 13 female; mean age 15.1 years; range: 11.5–18.3 years [Table 1]) were available. Birth, gender, racial background, dentition, and treatment details were recorded. When multiple cephalometric radiographs of a subject were available, only the ones taken prior to starting orthodontic treatment were used, which ensured that there were no data re-inclusions. For each subject with DS, the lateral cephalometric radiograph in occlusion of a skeletal and dental Class I unaffected control subject matched for age, racial group and gender was obtained from the normative growth collection of the Burlington Growth Center, Faculty of Dentistry, University of Toronto. Lateral cephalograms of the subjects with DS and their controls were traced and digitized by the same experienced digitizer using the Dentofacial Planner cephalometric software (Dentofacial Software, Toronto, Ontario, Canada). The cephalometric analysis described by Suri et al.[15] was expanded to include detail of the maxillary morphology (Figure 1; Tables 2 and 3). An intraclass correlation coefficient analysis applied to the measurements from repeated tracings of 16 randomly selected films, done 1 month apart, revealed a high level of repeatability of the method of the cephalometric analysis. The average intraclass correlation coefficient was 0.99, ranging

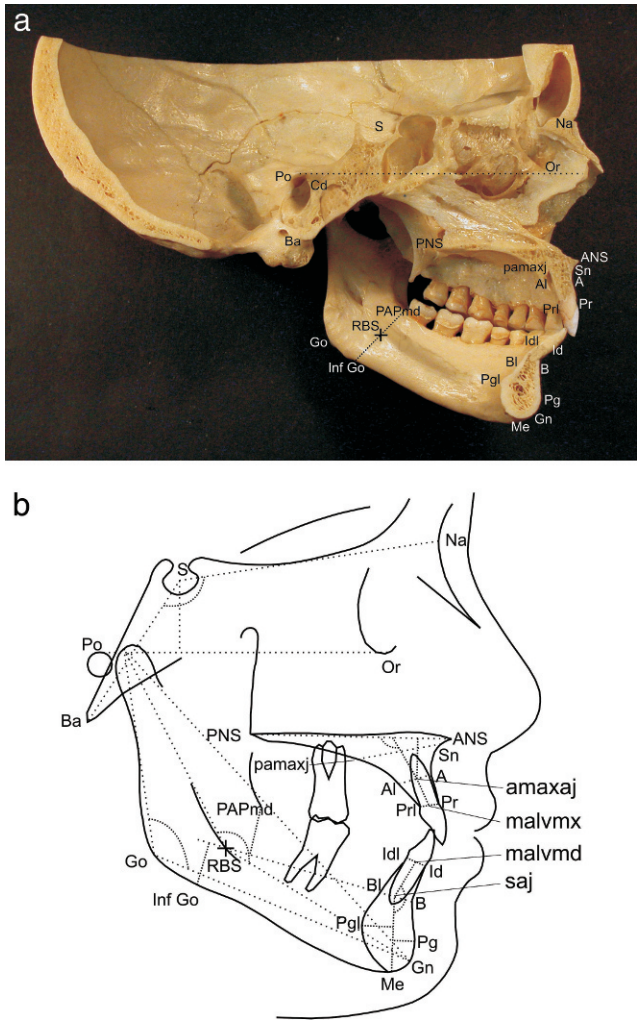

Figure 1. (a) Landmarks. (b) Measurements.

Table 2. Landmarks and Definitions Used in Cephalometric Analysis

Landmark	Definition
Conventional landmarks	
Ba	Basion
Na	Nasion
S	Sella
Po	Porion
Or	Orbitale
ANS	Anterior nasal spine
PNS	Posterior nasal spine
Sn	Subnasale
A	Subspinale (A point)
Pr	Prosthion
Co	Condylion
Go	Gonion
Me	Menton
Gn	Gnathion
Pg	Pogonion
B	Supramentale (B point)
Id	Infradentale
Idl	Lingual point infradentale
Specific landmarks used in this study	
Prl	Lingual prosthion
Al	Lingual A point
pamaxj (palate-anterior maxillary junction)	Most superoanterior point on palatal contour of basal anterior maxilla
mamax (midpoint of anterior maxillary base)	Midpoint of line drawn from pamaxj to Sn
amaxaj (anterior maxilla-alveolar junction)	Midpoint of a line drawn from Al to A
malvmx (midpoint of anterior alveolus, maxillary)	Midpoint of line drawn from Prl to Pr
PAPmd (posterior alveolar point, mandibular)	Most posteroinferior mid planed point on the anterior border of the ascending ramus
Inf Go (inferior gonion)	Mid planed point on the lower border of the mandible where the convexity at gonion merges with the concavity of the antegonial notch
RBS (ramus body syncline)	Point of intersection of a line drawn from Inf Go to PAPmd with the cortical outline of the mid planed mandibular nerve
Bl (lingual point B)	Point of intersection of a line drawn from RBS to B with the lingual contour of the symphysis
saj (symphysis-alveolar junction)	Midpoint of a line drawn from Bl to B
Pgl (lingual point pogonion)	Most prominent point on the lingual contour of the symphysis, as located by the greatest perpendicular distance from a line drawn from saj to Me
malvmd (midpoint of anterior alveolus, mandibular)	Midpoint of line drawn from Id(l) to Id

from 0.91 to 0.99. No adjustment for the similar radiographic enlargement (9.66% for the radiographs of the DS group acquired at the hospital and 9.84% for the Burlington control group, acquired at the Faculty of Dentistry, University of Toronto) was done. The null hypothesis was that there is no difference between the measurements of the DS group and normal controls. The cephalometric measurements recorded from the DS and control groups were analyzed using a paired *t*-test.

RESULTS

Almost all patients with DS (23 of the 25) were congenitally missing one or more permanent teeth as noted from an assessment of their available longitudinal panoramic radiographs. The average number of missing teeth per affected subject was 4.74. Details of the comparison of cephalometric measurements are provided in Table 4, and superimpositions of the average tracings of the two groups are illustrated in Figures 2 and 3. Varying degrees of deficiencies were found in the size and spatial relationships of craniofacial structures in the DS group in general. Both anterior and posterior face heights were reduced by 12.7% and 10.7%, respectively. Their upper anterior face height was smaller by 13.3%, while their lower anterior face height was smaller by 11.1%. These differences were very highly significant ($P < .001$). The face height ratio and Jarabak ratio were not significantly altered.

Table 3. Linear and Angular Measurements Made in Cephalometric Analysis

Measurement	Description
Anterior cranial base length	Length of the line drawn from S to N
Posterior cranial base length	Length of the line drawn from Ba to S
ST elevation to FHP	Perpendicular distance from S to FHP
Cranial base angle	Internal angle Ba-S-Na
Maxillary length	Length of the line drawn from PNS to ANS
Maxillary anterior basal width	Length of the line drawn from pamaxj to Sn
Maxillary anterior apical width	Length of the line drawn from Al to A
Anterior maxillary height	Length of perpendicular dropped from amaxaj to PNS-ANS
Maxillary anterior alveolar height	Length of line drawn from amaxaj to malvmx
Palatal/anterior maxillary deflection	Internal angle between the palatal plane (ANS-PNS) and line drawn from amaxaj to mamax
Mandibular length	Length of the line drawn from Co to Gn
External ramal length	Length of the line drawn from Co to Go
Internal ramal length	Length of the line drawn from Co to RBS
External body length	Length of the line drawn from Go to Gn
Internal body length	Length of the line drawn from RBS to Gn
Gonial angle	Internal angle Co-Go-Gn
Internal mandibular deflection	Internal angle Co-RBS-Gn
Mandibular posterior alveolar height	Length of the perpendicular dropped from PAPmd to RBS-B
Mandibular posterior body height	Length of the perpendicular dropped from Inf Go to RBS-B
Mandibular anterior alveolar height	Length of the line drawn from malvmd to saj
Symphyseal height	Length of the line drawn from the saj to Me
Symphyseal thickness	Sum of the lengths of perpendiculars dropped from Pg and Pgl to a line drawn from saj to Me
Mandibular plane/symphyseal deflection	Internal angle between Go-Gn and the line drawn from saj to Me
Ramal width	Length of the line drawn from the mid planed deepest points on the posterior and anterior borders of the ramus
Mandibular anterior apical base width	Length of the line drawn from Bl to B

All linear cranial base dimensions in the DS group were smaller than those of the control group. The anterior cranial base (S-N) was 13.6% smaller ($P < .001$), while the posterior cranial base (Ba-S) was smaller by 8.1% ($P < .001$). No significant differences were noted in the diameter of the pituitary fossa. The cranial base angle was much larger ($10.38^\circ \pm 5.77^\circ$; $P < .001$). Measured from the FHP, the sella turcica was strikingly lower (by 20%) in the DS group.

Nearly all maxillary measurements were smaller in the DS group, and the differences were large and statistically highly significant. Maxillary length was 17.4% smaller, and deficiencies in anterior maxillary dimensions ranged from 11.4% to 18.7%. The SNA angle was not significantly different. The relative inclination of the palatal plane to the SN was not significantly different, but it was rotated upwards anteriorly by almost 3° when measured to the Ba-N. The anterior maxilla was proclined by 8.9° relative to the palatal plane.

Mandibular analysis revealed a 6.9% smaller mandibular length (Co-Gn) in the DS group ($P < .001$) contributed by both a smaller mandibular body and ramus, while the ramal width was not significantly different. Both the posterior and anterior mandibular alveolar heights were smaller in the DS group by 25.5% ($P < .001$) and 12.5% ($P = .017$), respectively, while the posterior mandibular body height was not significantly different. The DS subjects also showed a thinner symphysis (by 13.8%; $P < .001$) with reduced height (by 8.4%; $P = .038$). Their symphysis was proclined by $6.11^\circ \pm 9.07^\circ$ to the mandibular plane ($P = .003$). Differences in other mandibular measurements, including the internal mandibular deflection angle and gonial angle, were not significant. The SNB angle was $3.67^\circ \pm 4.49^\circ$ larger in the DS group ($P = .001$). Measured to the SN plane, the mandibular plane angle was similar in both groups, but when measured to the FHP, was reduced by 4° in the DS group ($P = .009$).

Analysis of dentition revealed undereruption of the maxillary and mandibular incisors and molars in the DS subjects, with the maxillary incisors being most severely undererupted (by 6.29 mm). Their maxillary incisors were also more proclined to the palatal plane (by $6.88^\circ \pm 8.98^\circ$; $P = .001$). The DS group had on average a small anterior crossbite, although there was considerable variation (-0.26 ± 2.96 mm), while the control group had a normal overjet with much less variation (2.52 ± 1.09 mm). Similarly, the mean overbite in the control group was 3.84 mm deeper and again, there was a larger variation of the shallow bite depth in the DS group (0.25 ± 2.53 mm) in comparison with the bite depth recorded in the control

Table 4. Comparison of Skeletal and Dental Measurements of Down Syndrome (DS) Group vs Control Group

Measurement	DS Group (N = 25)		Control Group (N = 25)		
	Mean	SD	Mean	SD	Paired *t*-Test
S-N, mm	64.97	3.52	75.17	3.74	<.001***
Ba-S, mm	44.46	3.05	48.40	3.01	<.001***
Ba-N, mm	103.08	5.13	112.48	5.30	<.001***
Cranial base angle (S-N/Ba-S), degree	140.31	3.75	129.92	4.06	<.001***
Pituitary fossa, mm	10.74	2.12	10.24	3.34	.13
ST elevation to FHP, mm	15.90	3.13	20.56	3.72	<.001***
S-N/Maxillary plane, degree	8.53	2.39	8.22	2.96	.68
Ba-N/Maxillary plane, degree	24.50	2.37	27.47	2.66	.001**
S-N/Go-Gn, degree	28.61	6.31	30.34	4.50	.15
Ba-N/Co-Gn, degree	69.34	4.36	73.86	3.21	<.001***
FHP/Go-Gn, degree	20.32	6.39	24.41	5.32	.009**
N-Me, mm	106.23	8.04	121.74	6.00	<.001***
N-ANS, mm	47.42	2.89	54.65	3.01	<.001***
ANS-Me, mm	61.84	6.28	69.54	5.04	<.001***
S-Go, mm	70.36	5.88	78.83	6.45	<.001***
S-Go:N-Me, %	65.10	5.17	64.43	4.10	.54
N-ANS:ANS-Me, %	77.28	7.62	78.81	4.55	.37
SNA, degree	82.47	4.34	81.25	2.87	.22
SNB, degree	82.41	4.36	78.74	2.64	<.001***
ANB, degree	0.06	2.51	2.52	1.48	<.001***
Maxillary length, mm	47.80	3.77	57.90	3.76	<.001***
Palatal anterior maxillary deflection, degree	126.86	11.75	117.94	8.84	.006**
Maxillary anterior basal width, mm	18.25	3.49	21.22	2.90	.003**
Maxillary anterior apical width, mm	11.86	2.81	13.51	1.84	.010**
Anterior maxillary height, mm	7.78	1.18	9.58	1.50	<.001***
Maxillary anterior alveolar height, mm	9.29	1.71	11.68	1.70	<.001***
Co-Gn, mm	112.91	8.07	121.26	5.58	<.001***
Internal ramal length, mm	59.78	4.81	63.22	4.16	.014*
Internal body length, mm	57.39	5.46	62.43	3.71	<.001***
Co-Go, mm	54.81	4.98	58.72	5.33	.016*
Go-Gn, mm	75.21	6.60	79.72	4.74	.001**
Ramus/body ratio (internal)	1.05	0.10	1.02	0.09	.15
Ramus/body ratio (external)	0.73	0.06	0.74	0.08	.65
Ramal width, mm	32.88	3.93	33.60	3.28	.52
Mandibular posterior alveolar height, mm	10.50	2.09	14.09	2.25	<.001***
Mandibular posterior body height, mm	11.56	2.40	12.18	2.26	.44
Mandibular anterior alveolar height, mm	8.52	2.26	9.74	1.40	.017*
Mand ant apical width, mm	8.80	1.25	9.43	1.44	.14
Symphyseal height, mm	20.56	2.52	22.43	3.01	.038*
Symphyseal thickness, mm	13.41	1.54	15.56	1.90	<.001***
Internal mandibular deflection, degree	149.74	6.73	149.94	4.45	.90
Gonial angle, degree	121.68	6.50	123.12	4.95	.35
Mandibular/symphysis deflection, degree	75.93	7.63	69.82	5.34	.003**
Overjet, mm	−0.26	2.96	2.52	1.09	.001**
Overbite, mm	0.25	2.53	4.08	1.70	<.001***
Interincisal angle, degree	126.50	12.18	131.39	7.15	.11
U1_Maxillary plane, mm	24.04	3.14	30.33	2.38	<.001***
U1/Maxillary plane, degree	63.21	6.84	70.09	5.49	.001**
L1_Mandibular plane, mm	39.18	3.46	42.99	3.35	.001**
L1/Mandibular plane, degree	92.85	7.63	93.18	5.72	.87
Symphysis incisor angle, degree	16.92	6.48	23.37	6.48	<.001***
U6_Maxillary plane, mm	21.90	2.59	24.87	1.70	<.001***
L6_Mandibular plane, mm	29.59	3.08	32.53	3.79	.017*

* $P < .05$; ** $P < .01$; *** $P < .001$.

group (4.08 ± 1.70 mm). An anterior open bite or open bite tendency was frequently seen in the DS group. In fact, 52% of the patients in the DS group had an overbite of less than 1 mm or an open bite, and 48% had an anterior crossbite. In contrast, all subjects in the control group had positive overjet and only one had an overbite slightly smaller than 1 mm. It was qualitatively evident from the tracings that the tooth lengths were significantly smaller in the DS group (Figures 2 and 3).

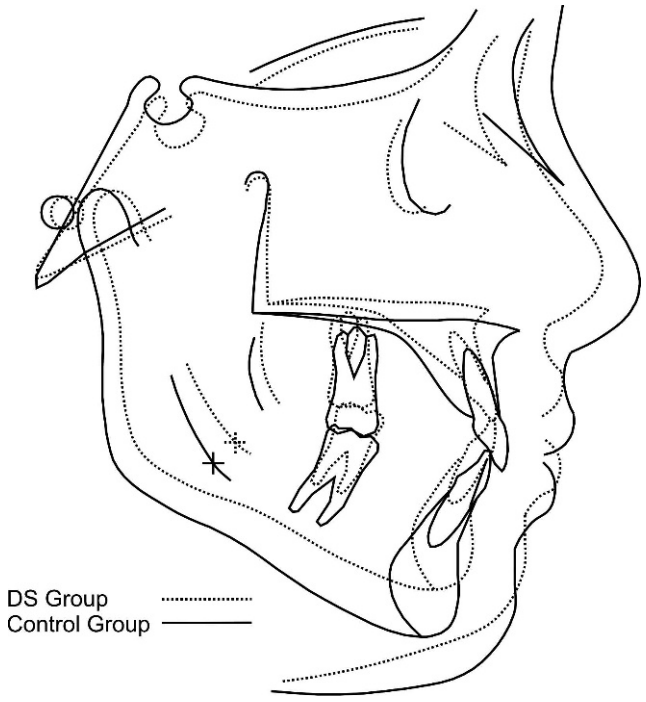

Figure 2. Cephalometric superimposition of average tracings of Down syndrome group on control group (FHP at Pt point). + represents location of RBS (ramus body syncline).

DISCUSSION

The null hypothesis was rejected. Our cephalometric analysis revealed that there was clear evidence of significant hypoplasia in endochondral, mesodermal, and ectomesenchymal derived structures of the cranium and face in the Down syndrome sample in comparison with their matched normal controls.

Our findings provide a more complete understanding of the underlying craniofacial morphologic features in DS because many of the differences with their closely matched controls we describe here have not been reported before. We found a significantly shorter mandible and mandibular ramus and body length in the DS group, which was unclear from previous studies.[6,8,9] We additionally found markedly reduced dimensions of the mandibular alveolar height and a relatively smaller, and more proclined symphysis. Our analysis also detected a narrower anterior maxillary base and anterior maxillary apical width. By demarcating the alveolar portions of the maxilla and mandible from their basal portions, we found severely reduced vertical maxillary and mandibular alveolar dimensions, which are explained by the hypodontia and reduced tooth eruption. The proclined and undererupted maxillary incisors and undererupted lower incisors promoted an anterior open bite. The tooth lengths in the DS group were qualitatively observed to be smaller, and this further contributed to reduced alveolar dimensions and anterior open bite.

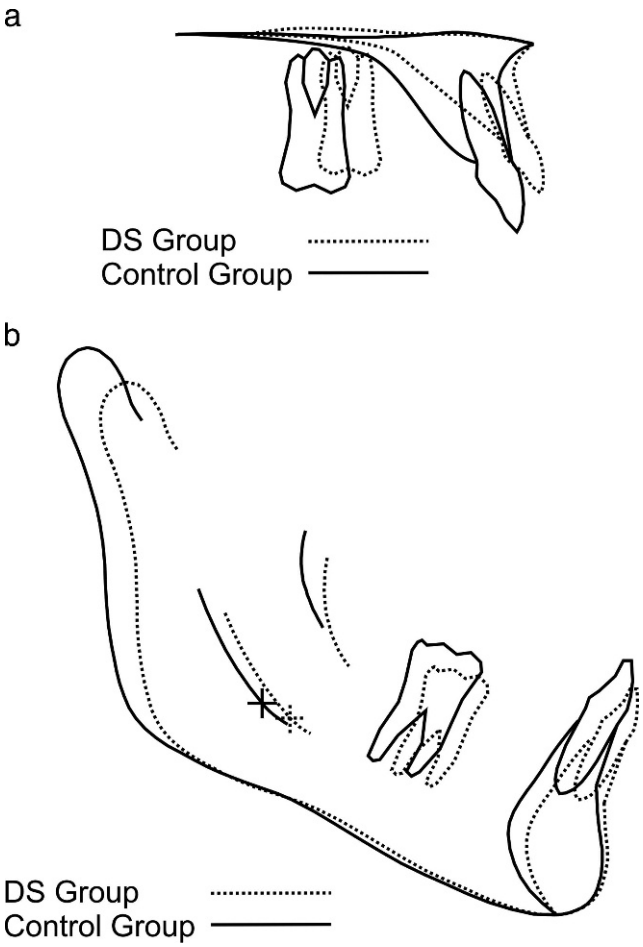

Figure 3. (a) Maxillary superimposition (maxillary plane at ANS). (b) Mandibular superimposition at T1 (mandibular plane at symphysis). + represents location of RBS.

Even though anterior open bite was found to be a common feature in the DS group, we found the mandibular plane angle to be significantly overclosed when measured to the FHP. In fact, inclinations of both maxillary and mandibular planes measured to the Ba-N and FHP were significantly decreased (Figure 2). However, similar reductions in the anterior and posterior facial heights led to similar Jarabak ratios. The severely shortened cranial base length in the DS group caused the SNA value to be similar to that in the control group due to a geometric effect, even with their small and retruded maxilla. This also led to the value of the SNB being relatively larger in spite of smaller mandibular dimensions. Mandibular overclosure (evident from the decreased mandibular plane angle measured to the FHP) further increased the relative mandibular prognathism. Gosman and Vineland[16] attributed progressive mandibular postural prognathism in DS to macroglossia. The small, retruded maxilla and relatively prognathic mandible led to a smaller ANB. These findings agree with those of Fischer-

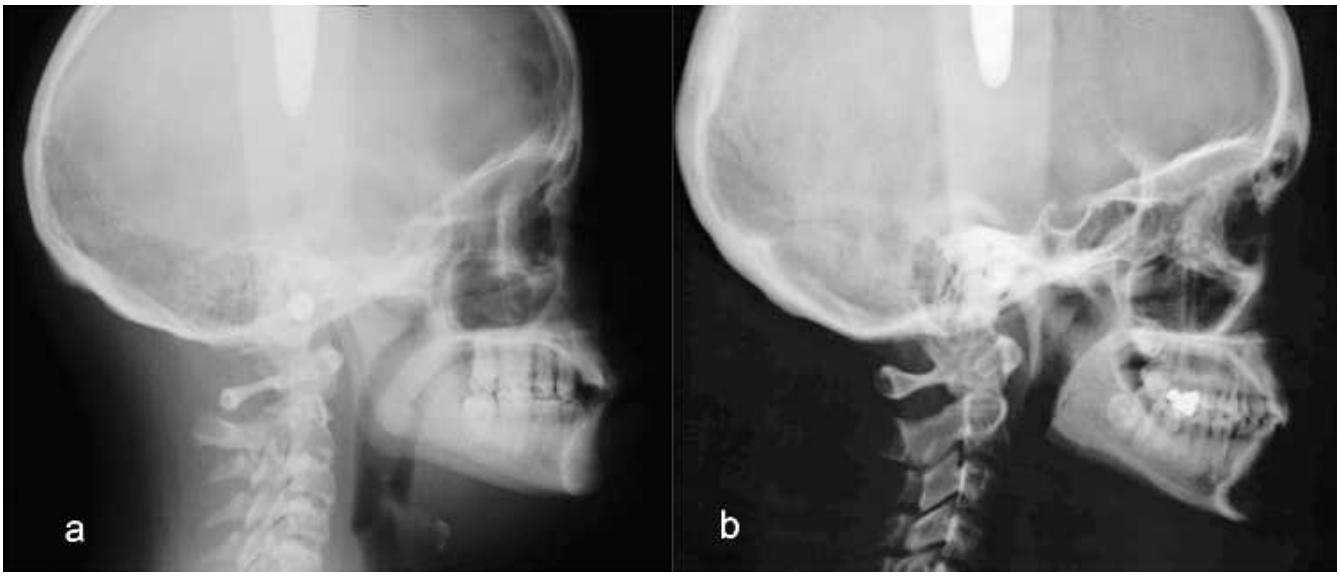

Figure 4. (a) Cephalograms of a child with Down syndrome and (b) control of similar age and gender. Note poor vertical sphenoid development and significantly lower vertical position of sella in (a).

Brandies,[8] although we found a distinctly smaller mandible in our DS sample but did not find the small decrease in the gonial angle to be significant.

Although the pituitary fossa diameter was normal in our DS sample, we found a marked degree of platybasia, exhibited by the cranial base angle being 140.3° ± 3.75°, which was 10° larger than the controls. This difference is twice as large as other reports have described.[3,5,7,8,12,17–19] Alio et al.[18] in a longitudinal study recently reported that in comparison with matched normal controls, the cranial base angle in DS actually increased during the 8–11 year period and then reduced slightly in annual decrements similar to those seen in their matched controls during adolescent growth. Various reasons that have been ascribed to the increased cranial base angle in DS include reduced prenatal vertical growth of the neuro-osteological cerebellar field,[17] lessened cerebral growth,[20] vertical hypoplasia of the central parts of the skull with reduced elevation of the sella,[8,21,22] and delayed ossification of the intersphenoidal synchondrosis.[23] We found the vertical position of sella from the FHP to be 20% lower in the DS group (Figure 4a,b). This finding supports the argument that the platybasia in DS is probably related to inadequate elevation of the sella during cranial base development, which occurs as a part of the entire cranial base-midface hypoplasia seen in DS.[8,21,22]

Deficient cranial base and midfacial growth in DS have been described to occur even prenatally in studies based on mouse DS models[24] and aborted human fetuses.[17] Insufficient endochondral growth at the synchondroses has been described to be the cause of the deficit since no evidence of their premature ossification has been found.[21] According to Sperber,[25] the attachment of the facial skeleton anteroinferiorly to the cranial base determines the chondrocranial influence on facial growth. This to some extent explains the relatively similar quantitative reductions seen in the maxilla and the anterior cranial base. Russell and Kjaer[26] hypothesized a possible association between growth around the sella turcica and innervation determined occurrence of tooth agenesis due to the close proximity of the cranial base with the trigeminal ganglion, and this interesting possibility should be explored further. In our sample, 92% of the subjects with DS exhibited hypodontia in some form.

Craniovertebral instability has been reported to occur with a relatively high frequency of 10%–20% in individuals with DS.[27,28] Whether differences in the severity of the platybasia along with a short Ba-S distance in DS are associated with differences in risk of craniovertebral injury or related complications needs to be explored. Although there are no reports of such injuries arising during orthodontic procedures, orthodontists should be aware of this important consideration and take precautions to prevent their patients with DS from overextending or overflexing the neck during treatment procedures.

Fisher-Brandies[8] reported that the maxillary plane in DS was unaffected in its inclination to the SN plane since it was similar to that of unaffected subjects. Although we too did not find a significant difference in maxillary plane inclination to the SN plane, there was a significant 3° anterior upward inclination of the maxillary plane when measured to Ba-N. We interpret that mandibular and maxillary plane inclinations in DS are better evaluated in relation to the FHP rather than the

SN plane, which may be misleading due to the cranial platybasia, with the sella turcica being in a relatively lower position. These considerations are important while planning orthodontic treatment and orthognathic surgery for patients with DS.

Individuals with DS are frequently the victims of a stereotype image that has come to be associated with their condition. A good orthodontic treatment result is certainly possible in patients with DS.[29–31] The need for including orthodontic management of patients with DS in orthodontic residency programs as well as more frequent scholarly reports in the orthodontic literature have been mooted to increase the awareness and comfort level of orthodontists in handling the clinical care of individuals with DS.[32] We hope that this comprehensive cephalometric appraisal elucidating the craniofacial features in DS will augment steps in this direction.

CONCLUSIONS

- Platybasia, revealed by a cranial base angle that was more obtuse by 10° and a relatively inferior position of the sella, was noted in the subjects with Down syndrome.
- The alveolar heights of their maxilla and mandible were reduced.
- Their maxillary length and anterior maxillary dimensions were smaller.
- Their mandibular ramus, body, and symphyseal dimensions were smaller.
- Their more proclined and undererupted maxillary incisors and undererupted lower incisors promoted an anterior open bite.
- Forward rotation patterns of their maxillary and mandibular planes led to overclosure and promoted the relative mandibular prognathism.

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