ORIGINAL ARTICLE

The mandibular catch-up growth controversy in Pierre Robin sequence

John Daskalogiannakis, DDS, MSc,[a] R. Bruce Ross, DDS, MSc,[b] and Bryan D. Tompson, DDS, Dip Ortho[c]
Toronto, Ontario, Canada

The purpose of this retrospective longitudinal cephalometric study was to investigate differences in craniofacial and especially mandibular morphology between patients with Pierre Robin sequence and isolated cleft palates. The experimental group comprised 96 patients (54 males and 42 females) with a history of Pierre Robin sequence. This group was compared cephalometrically with a control group of 50 patients (25 males and 25 females) with a history of isolated clefting of the palate. All 96 patients in the PR group had a lateral cephalogram at a mean age of 5.5 years. Thirty-eight of those patients had additional cephalograms at the mean ages of 10.3 years and 16.8 years. All patients in the cleft palate group had 3 corresponding cephalograms at the following mean ages: 5.7 years, 10.6 years, and 17.0 years. Twenty-nine cephalometric measurements were performed on each cephalogram with the use of computerized cephalometric software. Significant differences were identified between the 2 groups, particularly in the size and sagittal position of the mandible, which was consistently shorter in the Pierre Robin group at all 3 ages. Less severe differences were noted in the inclination of the palatal plane, the facial height proportions, and the midface depth. We conclude that patients with Pierre Robin sequence have a significantly smaller mandible as compared with patients with isolated cleft palate, and the difference does not change after the age of 5 years. (Am J Orthod Dentofacial Orthop 2001;120:280-5)

Pierre Robin (PR) sequence has come to signify the presence of mandibular retrognathia, cleft palate, and glossoptosis (backward falling of the tongue into the pharynx) in the newborn. Estimates of its prevalence vary from 1 in 8500 births[1] to 1 in 20,000.[2] Patients commonly exhibit upper airway obstruction and concomitant feeding difficulty that may be severe enough to necessitate a tracheostomy in the neonatal period.[3] Other suggested types of management include prone positioning of the infant,[4] mandibular traction and advancement appliances,[5] nasopharyngeal intubation,[6] tongue-lip adhesion,[7,8] and release of the musculature of the floor of the mouth.[9]

The term "sequence" (currently favored over the previously reported "syndrome" and "anomalad") reflects the prevailing concept that the mandibular micrognathia is the primary pathogenetic event, subsequent to which, the tongue, because of restricted space, interferes with fusion of the palatal shelves prenatally and obstructs the upper airway in the immediate postnatal and neonatal period.[10,11]

The etiopathogenesis of the mandibular micrognathia itself remains a matter of considerable debate. Some investigators have supported the compression (mechanical or positional) theory, according to which micrognathia of the mandible is the result of intrauterine molding against the sternum, possibly associated with oligohydramnios.[12-15] If this theory is accurate, it would appear logical to expect some rebound growth of the mandible shortly after birth, reducing the facial convexity and perhaps allowing the mandible to catch up with the maxilla.

A number of cephalometric studies have attempted to investigate this catch-up growth issue. Pruzansky[16] found the facial profiles of 21 patients with PR sequence to be nearly identical to those of patients with isolated cleft lip by the age of 10.5 years, although they had been much more convex at infancy.[16] Hotz and Gnoinski[17] reported that by the age of 5 years no difference in mandibular length existed between 7 patients with PR sequence and 7 patients with isolated cleft palate (CP). Figueroa et al[18] followed 17 infants with PR between 3 months and 2 years of age and compared them with 26 infants with isolated CP and 23 healthy infants of similar ages. Their finding of increased rate of growth in the PR group, as compared with the 2 other groups, was interpreted as partial mandibular catch-up growth, because the mandibular length in the

From the Division of Orthodontics, Department of Dentistry, The Hospital for Sick Children, Toronto, Ontario, Canada.
[a]Staff Orthodontist.
[b]Staff Orthodontist and Professor, Faculty of Dentistry, University of Toronto.
[c]Head of Division of Orthodontics and Associate Professor, Faculty of Dentistry, University of Toronto.
Reprint requests to: John Daskalogiannakis, Division of Orthodontics, Department of Dentistry, The Hospital for Sick Children, 555 University Ave, Toronto, ON, M5G 1X8, Canada; e-mail, jdask@hotmail.com.
Submitted, June 2000; revised and accepted, December 2000.

0889-5406/2001/$35.00 + 0 **8/1/115038**
doi:10.1067/mod.2001.115038

Table I. Sex and age distribution of Pierre Robin and cleft palate groups

	PR	*CP*
T1	N = 96 (54♂, 42♀)	N = 50 (25♂, 25♀)
	5.5 y (4.3-7.6*)	5.7 y (4.5-7.7*)
T2	N = 38 (20♂, 18♀)	N = 50 (25♂, 25♀)
	10.3 y (9.2-2.3*)	10.6 y (9.3-12.3*)
T3	N = 38 (20♂, 18♀)	N = 50 (25♂, 25♀)
	16.8 y (14.6-20.3*)	17.0 y (14.3-23.3*)

*Age range, in years.

PR sample still remained significantly shorter at the end of the observation period.[18]

On the other hand, Marcovic[19] found evidence of mandibular catch-up growth in only 1 of 15 PR patients between age 2 years and early adolescence. A number of more recent cephalometric investigations have concluded that PR patients remain more retrognathic and more convex than patients with CP into adulthood.[20-22]

This retrospective longitudinal cephalometric investigation was undertaken to compare differences in craniofacial and especially mandibular morphology between patients with PR sequence and isolated CP, in an attempt to shed some light on the mandibular catch-up growth controversy.

MATERIAL AND METHODS

The samples for this study were obtained from the patient database of the Hospital for Sick Children in Toronto, Canada. The patients in the PR group exhibited mandibular micrognathia, cleft of the secondary palate, and 1 or more incidents of severe respiratory distress in the neonatal period. The criteria for selection of patients for the control (CP) group were a history of complete (to the incisive foramen) or severe incomplete (well into the hard palate) isolated clefting of the palate. Patients diagnosed with other syndromes or with any associated anomalies were excluded from the sample. All palate repairs in both groups were performed in the same center, according to the same protocol with regard to timing, which included repair of the palate (soft and hard, excluding the alveolus) at the age of 12 to 18 months. Three different surgeons performed the repairs using 3 different techniques or modifications, but the distribution of the 3 surgeons in the 2 groups was approximately the same. None of the patients in either group underwent any orthognathic surgical procedure or functional appliance treatment during the experimental period, although many did have fixed appliance orthodontic treatment.

A cephalometric comparison between the 2 groups was performed at 3 different time registrations (T1, T2, and T3). At T1 the mean age of the 96 PR patients (54 males and 42 females) was 5.5 years. Thirty-eight of those patients (20 males and 18 females) had subsequent records and were reevaluated at T2 (mean age, 10.3 years), and at T3 (mean age, 16.8 years). The mean ages of the 50 patients (25 males and 25 females) that were followed serially in the CP group were 5.7 years at T1, 10.6 years at T2, and 17.0 years at T3. The distribution of the 2 groups is shown in more detail in Table I.

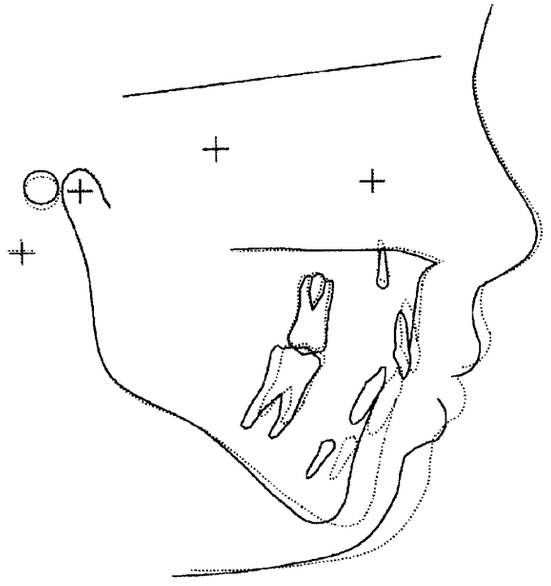

Fig 1. Superimposition of composite tracings of Pierre Robin group (*solid line,* N = 96) and cleft palate group (*dotted line,* N = 50) at T1.

All radiographs were traced and subsequently digitized by an experienced technician using the Dentofacial Planner cephalometric software (Dentofacial Software, Toronto, Ontario). A total of 68 points were digitized per tracing. The software is capable of determining the average location of each of these landmarks in a data set (ie, all patients of one group at a specific time registration), offering the possibility of composite (average) tracings for each of the groups at T1, T2, and T3. Twenty-nine hard and soft tissue cephalometric measurements (angular and linear) were performed. No dental measurements were evaluated at T3 because many patients from both groups had fixed appliance orthodontic treatment, which introduced an additional source of variability. The results were statistically evaluated by 3-way analysis of variance to test for differences due to group, sex, and time.

RESULTS

The superimpositions of the average tracings of the 2 groups at the 3 ages are shown in Figures 1 through 3.

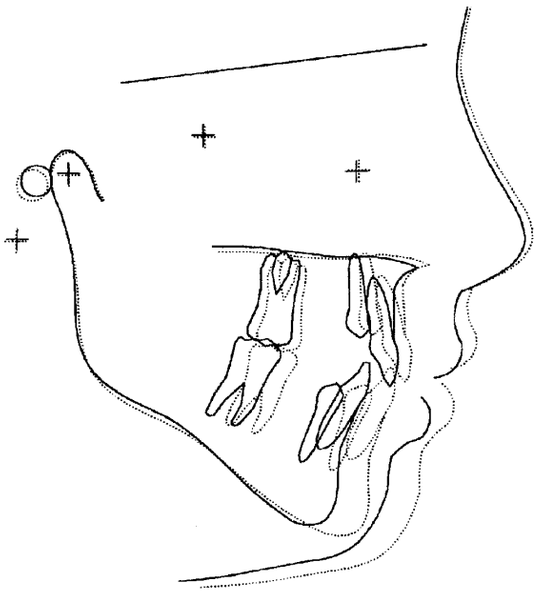

Fig 2. Superimposition of composite tracings of Pierre Robin group (*solid line,* N = 38) and cleft palate group (*dotted line,* N = 50) at T2.

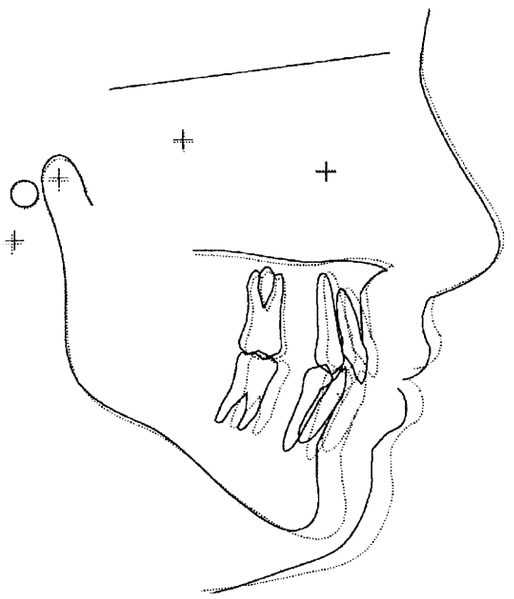

Fig 3. Superimposition of composite tracings of Pierre Robin group (*solid line,* N = 38) and cleft palate group (*dotted line,* N = 50) at T3.

No significant differences were detected between the sexes within each group at any time. The differences in the maxillary measurements (SNA, Ba-N-ANS) between the 2 groups were not significant, with the exception of the midface depth (Ba-ANS), which was significantly shorter in the PR group ($P < .05$).

The PR group had significantly smaller SNB and Ba-N-Pg angles ($P < .001$) and significantly larger ANB, ANS-N-Pg, and Wits values ($P < .001$) (Fig 4). These differences indicate a more retrognathic skeletal pattern due to a more severe mandibular retrognathism and shorter mandibular length ($P < .001$) at all 3 ages. The difference was also evident at the soft tissue level, with the PR group being significantly more convex ($P < .05$).

The mandibular plane (SN to GoGn) was significantly steeper ($P < .05$) in the PR group compared with the CP group, as was the palatal plane (SN to ANS-PNS).

Some significant differences were also found in the dentition; the PR group exhibited significantly larger overjet ($P < .001$), deeper overbite ($P < .001$), more retroclined maxillary incisors ($P < .05$), and more proclined mandibular incisors ($P < .05$).

The results are presented in detail in Table II.

DISCUSSION

Some authors have reported that many of the patients that carry the PR diagnostic label may in fact represent various other syndromes (eg, Stickler's, velocardiofacial) that are associated with a genetically induced mandibular micrognathia.[23,24] However the craniofacial morphology of all such syndromes has not been described adequately. For example, Selnes et al[25] recently reported that patients with velocardiofacial syndrome have mandibles of normal size. Nevertheless, extra care was taken in this study to exclude all known syndromic cases from the samples in an effort to minimize bias. It is reasonable to assume that in a large craniofacial center, where syndromologists and clinical geneticists are part of the craniofacial team, chances are that a known genetic syndrome will have been diagnosed by the age of 15 years.

The birth of a baby with PR sequence often constitutes a medical emergency in the delivery room. The clinically observed gradual improvement in respiration and feeding in the first few months or years of life, combined with some early cephalometric reports, has given support to the mandibular catch-up growth concept, which has come to be rather widely held.[26-29] This concept has led some authors to classify PR sequence among the few craniofacial deformities that improve with age.[11,16,26]

The findings of this investigation of a large sample of patients with PR sequence indicate that increased growth of the mandible in these patients does not occur after the age of 5 years. The mandibular length (Co-Gn) of the patients in the PR group was 4% to 5% shorter ($P < .001$) than that in the CP group, at all 3

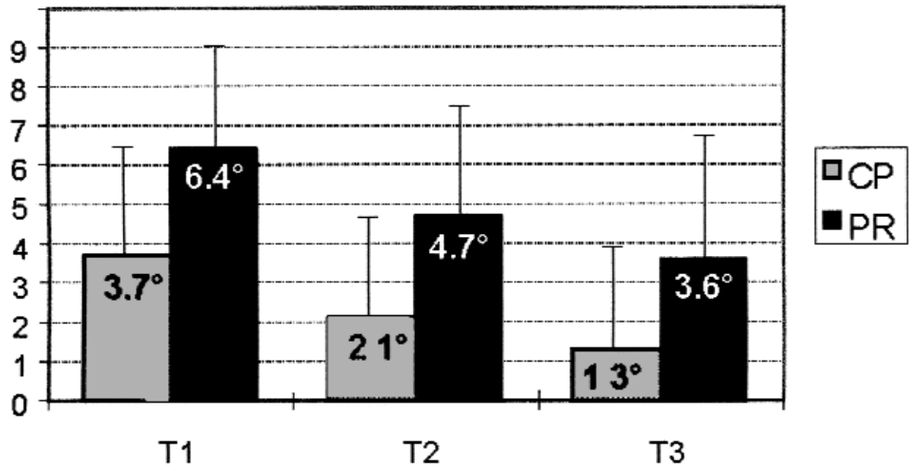

Fig 4. Differences in mean ANB angle between 2 groups at 3 ages ($P < .001$). *Error bars* indicate SD.

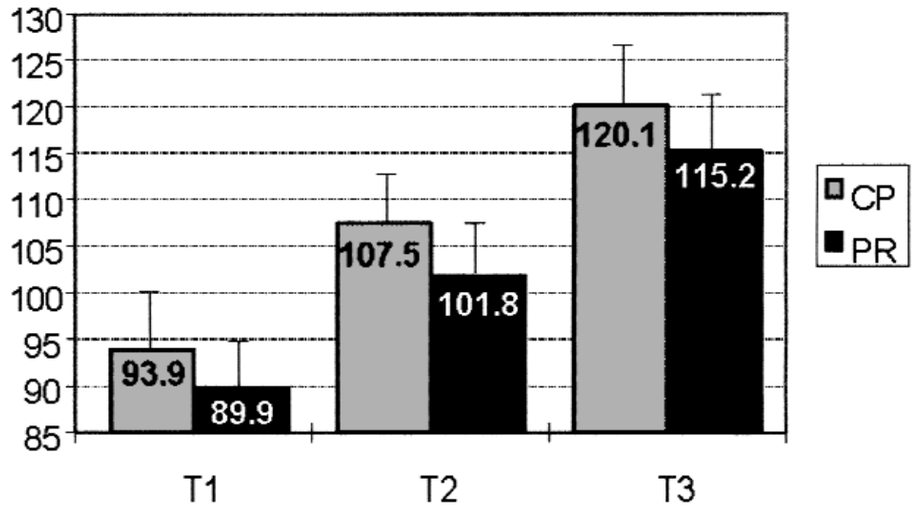

Fig 5. Differences in mean mandibular length (Co-Gn) between 2 groups at 3 ages ($P < .001$). *Error bars* indicate SD.

ages (Fig 5). None of the individual patients exhibited a significant improvement in their skeletal pattern that could be construed as a gradual correction of the initial severe Class II relationship.

It is conceivable that some degree of accelerated mandibular growth may occur in the immediate neonatal or postnatal period. However, considering also the findings of Figueroa et al,[18] such a growth spurt would appear to be rather limited, and it certainly does not result in harmonization of the facial profile. Our findings are in agreement with those of Ranta et al,[21] Laitinen and Ranta,[20] and Laitinen et al,[22] perhaps corroborating the hypothesis of an inherent mandibular micrognathia in PR sequence.

The implications of these findings are substantial. The development of techniques that offer the possibility of earlier treatment has created new dilemmas. Treatment of PR patients with new surgical approaches such as distraction osteogenesis may aid in early decannulation,[30] but it is sometimes avoided or delayed in the hope of spontaneous correction through mandibular catch-up growth.[31] The evidence from this study would support the decision of early treatment because spontaneous improvement through growth does not appear likely.

Table II. Cephalometric measurements, values, and statistical significance of differences between Pierre Robin and cleft palate groups at 3 time registrations

	T1		*T2*		*T3*		
Measurements†	*PR*	*CP*	*PR*	*CP*	*PR*	*CP*	*P*
Anteroposterior							
SNA	77.6	77.9	75.9	76.9	76.0	76.8	NS
SNB	71.2	74.2	71.2	74.9	72.4	75.5	***
ANB	6.4	3.7	4.7	2.1	3.6	1.3	***
Ba-S-N	129.7	130.5	130.4	130.3	129.9	130.0	NS
Ba-N (mm)	94.7	95.1	101.4	102.8	108.0	109.4	NS
Ba-ANS (mm)	84.9	86.3	90.3	93.0	96.6	98.8	*
Ba-N-ANS	63.7	65.1	62.8	64.5	63.2	64.2	NS
Ba-N-Pg	52.6	56.0	53.5	57.1	54.8	57.9	***
ANS-N-Pg	11.0	9.1	9.4	7.4	8.3	6.3	**
SN to ANS-PNS	11.5	10.1	13.2	10.6	13.4	10.8	**
SN to GoGn	41.5	38.8	40.8	37.7	39.0	36.8	*
Gonial angle	137.4	135.1	134.8	132.3	131.5	130.0	NS
Md length (Co-Gn) (mm)	89.9	93.9	101.8	107.5	115.2	120.1	***
Wits appraisal (mm)	3.7	0.3	1.7	–1.1	2.1	–0.3	***
Vertical							
N-ANS (mm)	43.3	42.9	50.4	49.8	55.8	54.9	NS
ANS-Me (mm)	60.0	59.5	63.9	65.0	71.3	72.8	NS
ANS-Me / N-Me (%)	61.6	60.8	59.1	59.4	58.9	59.0	NS
Dental‡							
Interincisal angle	148.1	149.8	141.3	141.5			NS
Overjet	3.7	2.4	4.5	2.6			***
Overbite	2.6	1.1	5.4	3.1			***
UI to SN	85.2	88.6	91.5	95.8			**
UI to ANS-PNS	96.6	98.7	104.6	106.4			NS
UI to NA	7.5	10.8	15.6	18.8			*
UI to NA (mm)	–1.3	–0.3	1.7	2.8			*
LI to GoGn	83.0	81.1	84.3	83.0			*
LI to NB	18.0	15.8	18.4	17.6			NS
LI to NB (mm)	2.1	1.4	2.5	2.5			NS
Soft tissue							
Nasolabial angle	119.4	111.5	115.7	113.1	114.0	111.0	NS
Soft tissue convexity	18.8	14.0	18.7	14.7	17.0	14.2	**

NS, not significant; **P* < .05; ***P* < .01; ****P* < .001.
†All measurements in degrees unless otherwise specified.
‡No dental measurements were performed at T3 to avoid bias from orthodontic treatment.
PR, Pierre Robin group; *CP,* cleft palate group.

CONCLUSION

This study indicates that the mandible in a child with PR sequence is significantly smaller than average at the age of 5 years, and maintains the same relationship to the maxilla and cranial base during subsequent growth. If there is any accelerated mandibular growth before the age of 5, it is not adequate to mask the skeletal Class II malocclusion and harmonize the profile.

The authors thank Ms Lynn Cornfoot for her assistance with tracing and digitizing the radiographs.

REFERENCES

1. Bush PJ, Williams AJ. Incidence of the Robin Anomalad (Pierre Robin syndrome). Br J Plast Surg 1983;36:434-7.
2. Tolarova MM, Cervenka J. Classification and birth prevalence of orofacial clefts. Am J Med Genet 1998;75:126-37.
3. Randall P. Micrognathia and glossoptosis with airway obstruction: the Pierre Robin syndrome. In: Converse JM, editor. Reconstructive plastic surgery. Philadelphia: WB Saunders; 1964. p. 1452-62.
4. Pashayan HM, Lewis MB. Clinical experience with the Robin Sequence. Cleft Palate J 1984;21:270-6.
5. Wada T, Ishi T, Sugai T, Molla MR, Matsuya T, Miyazaki T, et al. Mandibular traction for relieving respiratory distress in the Pierre Robin anomaly. J Maxillofac Surg 1983;11:187-90.

6. Singer L, Sidoti EJ. Pediatric management of Robin sequence. Cleft Palate Craniofac J 1992;29:220-3.
7. Douglas B. The treatment of micrognathia with obstruction by a plastic procedure. Plast Reconstr Surg 1946;1:300-8.
8. Routledge RT. The Pierre Robin syndrome: a surgical emergency in the neonatal period. Br J Plast Surg 1960;13:204-18.
9. Delorme R-P, Larocque Y, Caouette-Laberge L. Innovative surgical approach for the Pierre Robin anomalad: subperiosteal release of the floor of the mouth musculature. Plast Reconstr Surg 1989;83:960-6.
10. Jones KL. Smith's recognizable patterns of human malformations. 5th ed. Philadelphia: WB Saunders; 1997. p. 234-5.
11. Vig KWL. Orthodontic perspectives in craniofacial dysmorphology. In: Vig KWL, Burdi AR, editors. Craniofacial morphogenesis and dysmorphogenesis. Craniofacial Growth Series. Monograph 21. Ann Arbor: University of Michigan Center for Human Growth and Development; 1988. p. 149-83.
12. Harris JWS. Oligohydramnios and cortisone-induced cleft palate. Nature 1964;203:533-4.
13. Latham RA. The pathogenesis of cleft palate associated with the Pierre Robin syndrome. Br J Plast Surg 1966;19:205-14.
14. Poswillo D. Observations of fetal posture and causal mechanisms of congenital deformity of the palate, mandible, and limbs. J Dent Res 1966;45:584-96.
15. Walker BE. Effects on palate development of mechanical interference with the fetal environment. Science 1959;130:981.
16. Pruzansky S. Not all dwarfed mandibles are alike. Birth Defects 1969;5:120-9.
17. Hotz M, Gnoinski W. Clefts of the secondary palate associated with the "Pierre Robin Syndrome." Swed Dent J 1982;6[Suppl 15]:89-98.
18. Figueroa AA, Glupker TJ, Fitz MG, BeGole EA. Mandible, tongue and airway in Pierre Robin sequence: a longitudinal cephalometric study. Cleft Palate J 1991;28:425-34.
19. Marcovic M. Growth changes in cases of mandibular micrognathia. Trans Eur Orthod Soc 1972;133-45.
20. Laitinen SH, Ranta RE. Cephalometric measurements in patients with Pierre Robin syndrome and isolated cleft palate. Scand J Plast Reconstr Hand Surg 1992;26:177-83.
21. Ranta R, Laatikainen T, Laitinen S. Cephalometric comparisons of the cranial base and face in children with the Pierre Robin anomalad and isolated cleft palate. Proc Finn Dent Soc 1985;81:82-90.
22. Laitinen SH, Heliovaara A, Ranta RE. Craniofacial morphology in young adults with the Pierre Robin sequence and isolated cleft palate. Acta Odontol Scand 1997;55:223-28.
23. Cohen MM Jr. A critical review of cephalometric studies of dysmorphic syndromes. Proc Finn Dent Soc 1981;77:17-25.
24. Shprintzen RJ. The implications of the diagnosis of Robin sequence. Cleft Palate Craniofac J 1992;29:205-9.
25. Selnes JE, Ross RB, Tompson BD, Siegel-Bartelt J, Rossouw PE. Skeletal morphology in velocardiofacial syndrome: a cephalometric analysis. Cleft Palate Craniofac J. In press 2001.
26. Poswillo D. The aetiology and surgery of cleft palate with micrognathia. Ann R Coll Surg Eng 1968;43:61-88.
27. Poswillo D. The aetiology and pathogenesis of craniofacial deformity. Development 1988;103[Suppl]:207-12.
28. Gorlin RJ, Cohen MM, Levin LS. Syndromes of the head and neck. 3rd ed. New York: Oxford University Press; 1990. p. 700-5.
29. Haskins Olney A, Kolodziej P, MacDonald MR, Schaefer GB. Robin sequence. Ear Nose Throat J 1997;76:620.
30. Strohecker B, Lahey D. Mandibular elongation by bone distraction: treatment for mandibular hypoplasia with Robin sequence. Plast Surg Nurs 1997;17:8-10,15.
31. Poswillo DE. Malformation, microtia and growth of the mandible. In: Vig KWL, Burdi AR, editors. Craniofacial morphogenesis and dysmorphogenesis. Craniofacial Growth Series. Monograph 21. Ann Arbor: University of Michigan Center for Human Growth and Development; 1988. p. 91-7.