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REVIEW ARTICLE

Cleft extension and risks of other birth defects in children with isolated cleft palate

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Abstract

Objective. To study the risks of having other birth defects in children born with an isolated cleft palate (iCP) when the length of the cleft was taken into account. The hypothesis was that a newborn with an extensive cleft lesion may have an increased risk of other birth defects compared to a child with a less extensive cleft of the palate. ***Material and methods.*** All Caucasian children with iCP born between 1975 and 2005 in the southwestern region of Sweden were included. Data were collected from standardized medical records and the length of the cleft was checked on the pre-surgical dental cast for each child. ***Results.*** A total of 343 children were born with an iCP. The incidence was 0.64/1000 live births. Thirty-four percent of children with either a total or partial iCP had other birth defects. The risk was 1.7 times higher for a total compared to a partial iCP. The two most common birth defects were congenital heart disease and intellectual disability. Ear problems related to infections were registered in 43% of cases. Fifteen percent of the children had the Pierre Robin sequence, which was analyzed as a separate variable and not included as a birth defect. ***Conclusions.*** The length of the iCP was found to influence the risk of having another birth defect as the total palatal clefts were more often combined with other birth defects compared to partial clefts. Careful medical check-ups are important for newborns with iCP since they have increased risks of other birth defects.

Key Words: *Birth defect, incidence, isolated cleft palate, relative risk*

Introduction

Isolated cleft palate (iCP) is a common congenital anomaly characterized by a cleft involving only the secondary palate behind the incisive foramen [1]. The length may be total or partial.

The incidence in Sweden for any type of cleft lip and palate (CLP) during the period 1975–1992 was reported to range from 1.2 to 2.0/1000 live births [2]. The incidence values for the Nordic countries are similar [3–6] but vary around the world [7,8]. One of the lowest incidence values is 0.3/1000 live births, as reported among the black population in North America [9].

The incidence for iCP in Sweden has been reported to be 0.5–0.7/1000 live births [10,11]. In the study by Hagberg et al. [11], the incidence values were similar for different types of clefts, including the iCP, with the exception of the bilateral CLP, which were rarer. The most common type of cleft in Finland is the iCP, with the tendency of a higher frequency of in eastern than western Finland [12].

Milerad et al. [2] reported that 22% of children with iCP born in the region of Stockholm had associated malformations. A study in France showed that other birth defects were more common in infants with an iCP (46.7%) than in infants with a CLP (36.8%), or with an isolated cleft lip (13.6%) [13]. However, reports on correlations between the length of the iCP and risks for other birth defects have not been found.

Organs described as sites for other birth defects vary in different studies. In a study by Stoll et al. [13], the central nervous system and the skeletal system were the most common sites, followed by malformations in the urogenital and cardiovascular systems. In the

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study by Milerad et al. [2], malformations of the upper or lower limbs or the vertebral column were the most common (33%). Developmental disabilities and deafness have also been reported as the most frequent diagnoses in children with iCP [14]. In the same study, infants born with iCP had a diagnosed syndrome more often than those who had a CLP (50% and 30%, respectively).

The aim of this study was to calculate the risks of other birth defects when the cleft length of iCP was taken into account. The hypothesis was that a newborn with a more extensive cleft lesion may have an increased risk of other birth defects. The hypothesis was based on clinical experience.

Material and methods

The study material comprised the total sample of children with iCP born between 1975 and 2005 in the southwestern region of Sweden. Non-Caucasian children and children with submucous clefts were not included in the study. In this region all newborns with CLP are referred to and registered by the CLP team at the Sahlgrenska University Hospital in Gothenburg. They will receive continuous treatment until they are adults. Each child is longitudinally followed from 0 to 19 years of age using a standardized protocol. The CLP team is responsible for the treatment and no private surgical care is available. The team basically consists of plastic surgeons, orthodontists and speech pathologists. Other specialists such as an audiologist and a psychologist are consulted when needed. Sweden has a well-organized system for birth registration of all newborns. The number of total live births in the region was acquired from the Total Population Register (TPR), in order to calculate the incidence of iCP.

The requested information for the study was available from standardized written records and/or from the database maintained by the CLP team in Gothenburg. Information was collected on cleft diagnoses, length of cleft, gender, other birth defects and ear problems related to infections. The Pierre Robin sequence was separately recorded as a variable, i.e. it was not included in the birth defects.

The length of the cleft was checked for each patient by measuring at the cleft lesion shown on the child's initial dental cast (Figure 1). As a routine, pre-surgical dental casts are taken for each child with iCP before any surgery or pre-surgical treatment is performed. The initial diagnosis was either a total isolated cleft palate (TiCP) starting directly posterior to the incisive foramen (Figure 1A) or a partial isolated cleft palate (PiCP) (Figures 1B and 1C). The PiCP group was divided into two subgroups defined as follows: PiCP (h), when the partial cleft partly involved the hard palate (Figure 1B); and PiCP(s), when only the soft palate was involved (Figure 1C).

The Confidence Interval Analysis (CIA) program was used to calculate the incidence values [15]. Estimates of the relative risk (RR) were calculated by 2×2 tables using the same program. The confidence interval (CI) was set at 95% for all analyses. The CI for the RR suggests a significant difference when the lower limit is close to or above 1.0. The study was approved by the Regional Ethical Committee of Göteborg (149-08).

Results

In the southwestern region of Sweden, there were 535 320 live births between 1975 and 2005. Of these, 343 children were Caucasians born with iCP. They comprised the study group. There were 171 males (49.9%) and 172 (50.1%) females. The incidence of iCP was 0.64/1000 live births (CI = 0.58–0.71).

TiCP was very rare compared to PiCP in that there were only 34 children with TiCP (9.9%) and 298 with PiCP (86.9%). There were 11 (3.2%) unclear cases concerning the length of the cleft. The reason was

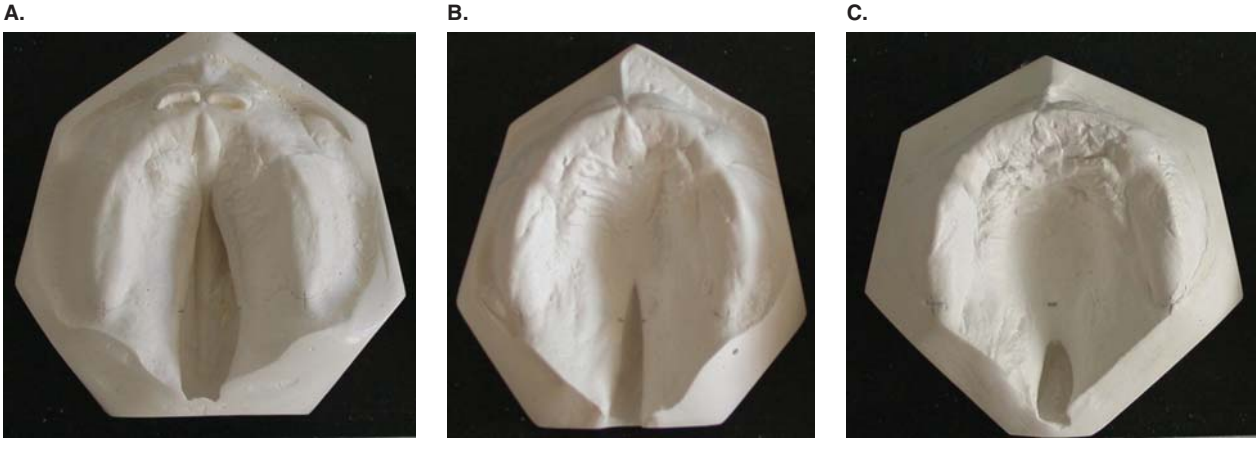

Figure 1. Diagnoses of iCP: (A) TiCP; (B) PiCP(h); (C) PiCP(s).

either a missing or a bad-quality dental cast. Among 298 children with PiCP, 161 (54%) had PiCP(h) and 137 (46%) had PiCP(s). The distributions between genders were similar (Figure 2). The incidence value for TiCP during the full study period of 31 years was 0.06/1000 live births (CI = 0.04–0.09). The corresponding value for PiCP was 0.56/1000 live births (CI = 0.50–0.62). The incidence values were similar when separate calculations for 10-year periods were carried out (Table I).

An iCP with a report of one or more birth defects except for the cleft was registered in 116/343 children (33.8%). The RR calculations regarding an iCP did not include the 11 cases with uncertain information about being total or partial. There were 64 males (55.2%) and 52 females (44.8%) with other birth defects (Table II). Among the children with iCP, there was no significant difference between males and females regarding other birth defects (RR = 1.24, CI = 0.92–1.67). The children with TiCP had a 1.7-times higher risk of having other birth defects compared to those who had PiCP (RR = 1.71, CI = 1.20–2.46), and a 1.78-times higher risk compared to those who had PiCP(h) (RR = 1.78, CI = 1.20–2.64). A comparison regarding a cleft partly involving the hard palate or only the soft palate showed no significant difference (RR = 1.07, CI = 0.78–1.46).

There was a large variation in birth defects. Congenital heart disease was recorded for 19% and intellectual disability for 18% of the children. Eighty-seven children (25%) had a diagnosed syndrome. There were 19 different diagnoses of syndromes and the two most common were Down's syndrome (n = 5) and 22q11 deletion syndrome (n = 4). Five cases were described only as chromosomal disturbances. Examples of other single syndromes were Treacher Collins, Wolg Hirschhorn, Robinow, Patau, Klinefelter, Beckwith–Wiedemann, Larsen and Binder syndromes. Birth defects commonly involving the following organ systems were reported: the extremities and skeletal system; the cardiovascular system; the respiratory system; the urogenital system; the gastrointestinal system; the central nervous system; the eye; and the ear.

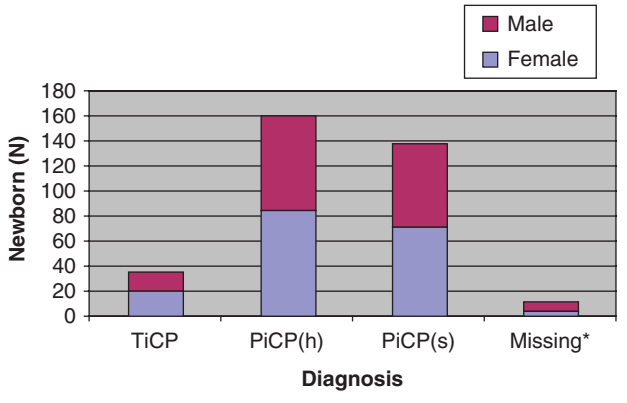

Figure 2. Distribution between genders in the different diagnoses of iCP. Missing = unclear cases of iCP diagnosis due to a missing or bad-quality dental cast model.

The results revealed that 52 (15.2%) of the children in the total sample group had the Pierre Robin sequence and the incidence of this combination was 0.10 (CI = 0.07–0.13). There were 21 males (40.4%) and 31 females (59.6%) within this group (Table II). No difference based on gender and a diagnosis of the Pierre Robin sequence was found (RR = 0.68, CI = 0.41–1.14). The risk of having the Pierre Robin sequence in the children born with a cleft involving both the hard and soft palates, relative to a cleft only in the soft palate, was significantly higher (RR = 2.05, CI = 1.14–3.70).

In the total study group, 149 children (43.4%) had repeated episodes of ear problems related to ear infections during childhood. The distribution between genders was almost equal (74 males, 75 females). Seventeen patients had no recorded information on this matter.

Discussion

The study sample was regarded as being complete with the exception of children born with submucous clefts. They could not be included due to the difficulty of an early diagnosis and unclear information regarding the length of the palate. These children do not follow the standardized registration system. The number of iCPs (n = 11) that were excluded from the calculation of risks because of the difficulty of precisely checking the length of the cleft was small and was not likely to affect the results.

The incidence of iCP was 0.64/1000 live births. This value is similar to a report for the county of Stockholm (0.7/1000) [11] and to the value from the WHO registry for Northern Europe (0.59/1000) [1]. The time-trend information was derived from the calculation of three 10-year incidence intervals. These incidence values did not show any significant changes between 1975 and 2005 (Table II). This is somewhat different from Mossey [16], who reported a progressive increase in palatal clefts in Finland and Norway during the period 1980–1994. These variations in incidence values have been discussed as being dependent on the sources of records, unspecific information such as live birth or termination and the length of the study period [16,17]. In the present study, information on fetal deaths and termination of pregnancies was not available and the results only concern live births.

There were similar distributions of iCP between boys and girls. This differs from the results of Hagberg et al. [11] and Mossey [16], who revealed that iCPs were found slightly more often among females compared to males.

Table I. Numbers of total live births and incidence of iCP per 1000 live births in the southwestern region of Sweden over 10-year periods.

Time period	Total live births	iCP	Incidence	95% CI
1975–1984	161 951	100	0.62	0.50–0.75
1985–1994	195 278	134	0.69	0.58–0.81
1995–2005	178 091	109	0.61	0.50–0.74
1975–2005	535 320	343	0.64	0.58–0.71

Table II. Numbers and frequencies of other birth defects in the total sample of children with iCP ($n = 343$) and for the extension of the TiCP, PiCP(h) and PiCP(s) ($n = 332$).

	Birth defect; *n* (%)	No birth defect; *n* (%)
Total sample	116 (34)	227 (66)
Males	64 (19)	107 (31)
Females	52 (15)	120 (35)
TiCP/cast model	18 (5)	16 (5)
PiCP(h)/cast model	48 (14)	113 (34)
PiCP(s)/cast model	44 (13)	93 (28)
Missing cast model	6 (2)	5 (2)

Thirty-four percent of children with iCP had at least one other birth defect. Earlier reports on frequencies of malformations ranged from 22% to 71% [18–22]. The two most common birth defects in the present study were congenital heart disease and intellectual disability. These have also been reported as being common in other investigations [19,22]. In the study by Milerad et al. [2], a congenital heart disease was reported as the most common isolated associated malformation. However, in the referred studies, combinations of other types of clefts were also included.

The registration procedures and the CLP team records follow a standardized protocol that has not been changed over the years. The youngest children were born in 2005 and it is not likely that many birth defects would have remained undiscovered at the age of 3 years, although the diagnosis may initially have been missed. For example, intellectual disability could be detected in an older child [22]. Our interest was focused on the presence of birth defects, without grading their severity. Definitions and classifications of syndromes may vary. Autopsies to ensure a correct diagnosis are not always performed. The variation in type of birth defect varied widely but resembled a previously published detailed report on this matter for children with CLP in the greater Stockholm area of Sweden [2].

It is interesting to see that the children with TiCP had a 1.7-times higher risk of having other birth defects compared to those with PiCP. The PiCP group included both children with a partial cleft extending into the hard palate and those with a cleft only in the soft palate. This result confirmed our hypothesis that the children who had a longer cleft lesion had a higher risk of having an additional malformation. A suggested explanation is that a total cleft develops earlier than a partial cleft. Generally, the risk of severe disturbances in the fetus is highest in the first trimester [23].

We collected information regarding the Pierre Robin sequence as a separate variable. This abnormality could have subsided when the baby was grown up and we chose not to include it as another birth defect since it is related to iCP. iCP and micrognathia and/or retrognathia of the mandible cause the tongue to be displaced in a posterior position leading to various degrees of breathing problems. The primitive tongue is recognized early in the fourth or fifth week of gestation. It can then act as a mechanical barrier during fusion of the palatal shelves [24]. In the present study, the relative risk of having the Pierre Robin sequence and a cleft involving both the hard and soft palates was two times higher than with a cleft only in the soft palate. The growing tongue, if positioned very early during fetal growth into the cleft area, could possibly affect the fusion of the palatal shields to a larger extent, leading to a longer extension of the iCP.

Nearly half of the children had repeated episodes of ear problems related to infections. This result may be underestimated, since parents often seek treatment for their children at local hospitals and do not inform the CLP team. An Irish study revealed that the parents of children registered in a CLP unit reported ear problems in 71% of cases. Forty-five percent of children with cleft lip or CLP had a history of recurrent ear infections according to their medical records [25]. This value is in line with the present investigation.

Conclusions

This study included all children born with iCP in the region of southwestern Sweden over a 31-year period. The length of the isolated cleft was found to influence the risk of having another birth defect. Total palatal clefts were combined with other birth defects more often compared to partial clefts involving either the hard palate or only the soft palate. Careful medical check-ups are important for newborns with iCP since they have increased risks of other birth defects. Almost every third child with iCP had one or more other birth defects. The incidence of iCP was within the range for previously published reports for Caucasians.

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References

[1] Mossey P, Castilla E. Global registry and database on craniofacial anomalies. Report of a WHO Registry Meeting on craniofacial anomalies. Brazil: World Health Organization; 2001.

[2] Milerad J, Larson O, Ph DD, Hagberg C, Ideberg M. Associated malformations in infants with cleft lip and palate: a prospective, population-based study. Pediatrics 1997;100: 180–6.

[3] Jensen BL, Kreiborg S, Dahl E, Fogh-Andersen P. Cleft lip and palate in Denmark, 1976-1981: epidemiology, variability, and early somatic development. Cleft Palate J 1988;25: 258–69.

[4] Rintala A, Stegars T. Increasing incidence of clefts in Finland: reliability of hospital records and central register of congenital malformations. Scand J Plast Reconstr Surg 1982;16:35–40.

[5] Abyholm FE. Cleft lip and palate in Norway. I. Registration, incidence and early mortality of infants with CLP. Scand J Plast Reconstr Surg 1978;12:29–34.

[6] Moller P. Cleft lip and cleft palate in Iceland. Arch Oral Biol 1965;10:407–20.

[7] Calzolari E, Bianchi F, Rubini M, Ritvanen A, Neville AJ. Epidemiology of cleft palate in Europe: implications for genetic research. Cleft Palate Craniofac J 2004;41:244–9.

[8] Schutte BC, Murray JC. The many faces and factors of orofacial clefts. Hum Mol Genet 1999;8:1853–9.

[9] Seskin MZ, Stark RB. The incidence of congenital defects. Plast Reconstr Surg 1961;27:261–7.

[10] Henriksson TG. Cleft lip and palate in Sweden. A genetic and clinical investigation. Uppsala, Sweden: The Institute for Medical Genetics, University of Uppsala; 1971.

[11] Hagberg C, Larson O, Milerad J. Incidence of cleft lip and palate and risks of additional malformations. Cleft Palate Craniofac J 1998;35:40–5.

[12] Saxen I. Etiological variables in oral clefts. Proc Finn Dent Soc 1975;71(Suppl 1–3):1–40.

[13] Stoll C, Alembik Y, Dott B, Roth MP. Associated malformations in cases with oral clefts. Cleft Palate Craniofac J 2000;37:41–7.

[14] Mitchell LE, Beaty TH, Lidral AC, Munger RG, Murray JC, Saal HM, et al. Guidelines for the design and analysis of studies on nonsyndromic cleft lip and cleft palate in humans: summary report from a Workshop of the International Consortium for Oral Clefts Genetics. Cleft Palate Craniofac J 2002;39:93–100.

[15] Morris AJ, Gardner JM. Epidemiological studies. In: Altman GD, Machin D, Bryant TN, Gardner JM, editors. Statistics with confidence. 2nd ed. British Medical Journal; 2000. p. 57–72.

[16] Mossey P. Epidemiology underpinning research in the aetiology of orofacial clefts. Orthod Craniofac Res 2007;10:114–20.

[17] Gundlach KK, Maus C. Epidemiological studies on the frequency of clefts in Europe and world-wide. J Craniomaxillofac Surg 2006;34(Suppl 2):1–2.

[18] Shprintzen RJ, Siegel-Sadewitz VL, Amato J, Goldberg RB. Anomalies associated with cleft lip, cleft palate, or both. Am J Med Genet 1985;20:585–95.

[19] Milerad J, Larson O, Hagberg C, Ideberg M. Associated malformations in infants with cleft lip and palate: a prospective, population-based study. Pediatrics 1997;100:180–6.

[20] Shaw GM, Carmichael SL, Yang W, Harris JA, Lammer EJ. Congenital malformations in births with orofacial clefts among 3.6 million California births, 1983-1997. Am J Med Genet A 2004;125:250–6.

[21] Vallino-Napoli LD, Riley MM, Halliday JL. An epidemiologic study of orofacial clefts with other birth defects in Victoria, Australia. Cleft Palate Craniofac J 2006;43:571–6.

[22] Stoll C, Alembik Y, Dott B, Roth MP. Associated malformations in patients with oral clefts. Am J Med Genet A 2007;143:2463–5.

[23] Friede H. Growth sites and growth mechanisms at risk in cleft lip and palate. Acta Odontol Scand 1998;56:346–51.

[24] Evans AK, Rahbar R, Rogers GF, Mulliken JB, Volk MS. Robin sequence: a retrospective review of 115 patients. Int J Pediatr Otorhinolaryngol 2006;70:973–80.

[25] Sheahan P, Miller I, Sheahan JN, Earley MJ, Blayney AW. Incidence and outcome of middle ear disease in cleft lip and/or cleft palate. Int J Pediatr Otorhinolaryngol 2003;67:785–93.