

## EPIDEMIOLOGICAL STUDY

# The incidence of cleft lip and palate in the Czech Republic in 1994–2008

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**Abstract:** *Objective:* To determine the incidence of nonsyndromic cleft lip and/or palate in the Czech Republic among infants born during 1994–2008 as well as to define the ratio per live births and sex ratios. Another aim was to determine whether there was any trend in the incidence in this time period.

*Design:* Retrospective study.

*Setting:* Prague Center for the Treatment of Congenital Facial Anomalies.

*Material and methods:* Data were collected from the National Birth Defects Register (Institute of Health Information and Statistics), the Czech Statistical Office and the Czech Health Statistics Yearbooks. The incidence, ratios per live births and sex differences were calculated. Possible trends in the data series were investigated.

*Results:* Totally 2417 infants with a cleft defect were found among 1 471 789 newborns in time period 1994–2008. The overall incidence was 1.64 per 1000 live births or 1 in 600 live births. The incidence of cleft lip was 0.39/1000, the incidence of cleft palate was 0.68/1000 and the incidence of cleft lip and palate was 0.57/1000. The ratio per live births was 1 in 2648 in cleft lip, 1 in 1801 in cleft lip and palate and 1 in 1505 in cleft palate. The incidence was much higher among male babies in cleft lip patients (male to female ratio 2.07) and in patients with cleft lip and palate (males to females ratio 1.85). The male to female ratio in cleft palate newborns was 0.92. No traceable trend was found in the incidence.

*Conclusions:* In the Czech Republic, every year approximately 170 infants with cleft lip and/or palate were born, the incidence was 1.64 per 1000 live born infants during considered period. Males were affected more frequently with isolated cleft lip and cleft lip and palate, on the other hand, in cleft palate patients, there was a slight dominance of females. Further long-term studies are necessary in order to elucidate reasons of the oscillations in incidence of cleft anomalies, to identify possible teratogens and to give a starting indication for planning health service resource requirements for this group of affected infants (*Tab. 3, Fig. 4, Ref. 51*). Full Text in PDF [www.elis.sk](http://www.elis.sk).

**Key words:** incidence, cleft lip, cleft lip and palate, cleft palate.

The epidemiology of cleft lip and/or palate (CL/P) is a field of study of a population teratology. The aim of this field of medicine is to find the average incidence of congenital birth defects in the studied population, time period and environment. Geographic origin, ethnic background and socio-economic status are some of the factors that may account for the wide variability seen in the clefting rates (1–3). Incidence also varies in different cleft types. Native Americans have one of the highest birth incidence of cleft lip (CL) and cleft lip and palate (CLP) followed by Asians and least common are CL and CLP in African-derived populations (4–5). The prevalence of cleft palate (CP), however, shows less variation by race and ethnicity (4).

The orofacial clefts are among the most common congenital birth defects in the Czech Republic and thus the knowledge of their incidence is of great importance (6). In 1960, the Ministry of Health founded the Institute of Health Information and Statistics, with the aim of collecting and processing medical data, including congenital birth defects in the National Birth Defects Register (NBDR). Nowadays the congenital birth defects detected by prenatal diagnostics, among spontaneous abortions over 500 g of weight, stillborns and children till the finished 15<sup>th</sup> year of age are registered, this gives the physicians enough time to diagnose even latent anomalies using additional techniques such as X-ray (7–8). Since 2009, the Czech NBDR has been a member of the European register of congenital anomalies called EUROCAT (European Network of Registers for the Epidemiologic Surveillance of Congenital Anomalies). Currently EUROCAT collects data from 43 registers in 20 states covering 29 % of European birth population (9–10). In spite of efforts, the data on the incidence of congenital birth defects still do not exist in many countries (11–14). On the other hand, according to the latest research in the Netherlands, the validity of the whole country register of the Dutch Association for Cleft Palate and Craniofacial Anomalies was very good (15). To report a patient with CL/P into the NBDR is obligatory, therefore the registry should include the vast majority of cleft cases born in

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**Acknowledgment:** The authors would like to thank Doc. Peterka for sharing his extensive knowledge and Ing. Kaspřikové for the accurate statistical analysis.

the Czech Republic in the time period studied. However, validity of the registry was not verified, further research in this area is recommended.

In studies on the incidence of CL/P, different definitions of the subgroups of clefts are encountered. Cleft lip, without or with cleft palate, must be distinguished from isolated clefts of the hard and soft palates because of different embryologic, etiologic and epidemiologic backgrounds (16, 5). Therefore, it is appropriate to divide the cleft anomalies into the two subgroups – cleft lip, with or without cleft palate and a cleft palate alone. Nevertheless, in order to compare our results with previous studies done on the population of the Czech and Slovak Republics, in the current study, we maintain partially the division of the cleft a categories into the three main groups – cleft lip, cleft palate and cleft lip and palate.

Several studies have focused on the incidence of CL/P in the Czech Republic in the past. The basic research in this field was done by Cerny et al (17). He reported the occurrence of CL/P as 2 per 1000 live births among the Czech population for the 1964–1983 period, presenting CL/P anomalies as a major health problem. Peterka et al in their study presented the incidence of CL/P in Bohemia (major part of the Czech Republic) between 1964 and 1992 oscillating around 1.74 per 1000 newborns (18). The incidence of CL/P in the former Czechoslovakia was also mentioned in the study of Grundlach and Mause published in 2006, where data extracted from scientific references published between 1960 and 2000 were displayed (19). The range of the incidence reported varied from 0.85 to 2.00 per 1000 live births.

The aim of the current study was to assess the incidence of nonsyndromic CL/P in the Czech Republic in the years from 1994 to 2008 as well as to define and compare the ratios per live births

and sex ratios in the subgroups of cleft anomalies. Another goal was to determine whether there was any change in the incidence in this time period compared to the previously published data.

## Material and method

A retrospective study was undertaken to identify cleft lip and palate births in the Czech Republic in the years from 1994 to 2008. All data were gathered from the National Birth Defects Register (Institute of Health Information and Statistics) and the Czech Statistical Office (20–34). The absolute numbers of individuals with CL/P born each year were obtained, specifically noting the cleft type and the gender of the infant. Excluded were CL/P patients with associated syndromes, except Pierre Robin's.

A single operator was used to shift and record the data in a standardized format into the created computer database. The incidence of CL/P, CL, CLP and CP each year and in the whole time period was calculated, also for males and females separately, and outlying values were identified. Results were displayed graphically. Also, the male-to-female ratios were calculated and possible trends in the incidence were identified by the means of linear regression model.

## Results

From the total 1471789 live born infants born in the Czech Republic in the 1994–2008 time period, 2417 new cases of CL/P were reported. The overall incidence of cleft births over this 14 year period was 1.64 per 1000 live births ( $\sigma$  0.08) or 1 in 600 live births. The incidence of CL/P varied from year to year, ranging from 1.32/1000 in year 1996 to 1.95/1000 in 2008 with no trace-

**Tab. 1. Cleft subgroups share in the Czech population between years 1994–2008, absolute numbers, percentage, incidence per 1000 live births, ratio per live births (one in all live births) and sex ratio male to female.**

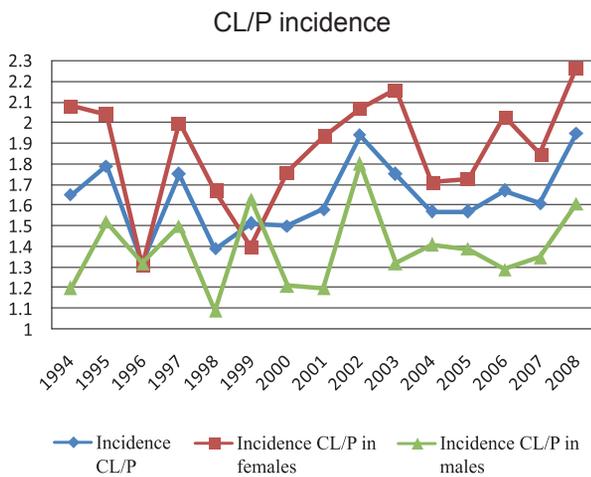
Type	n	%	Incidence per 1000 live births	Type	n	%	Incidence per 1000 live births	Ratio per live births	Sex ratio
CLP+CL	1415	59%	0.96 ( $\sigma$ 0.12)	CL	573	40.5%	0.39 ( $\sigma$ 0.07)	1/2648	2.07
				CLP	842	59.5%	0.57 ( $\sigma$ 0.1)		
CP	1002	41%	0.68 ( $\sigma$ 0.1)	CP	1002	100%	0.68 ( $\sigma$ 0.1)	1/1505	0.92
CL/P	2417	100%	1.64 ( $\sigma$ 0.08)	CL/P	2417	100%	1.64 ( $\sigma$ 0.08)	1/600	1.47

CL = cleft lip, CLP = cleft lip and palate, CP = cleft palate, CL/P = cleft lip and/or palate,  $\sigma$  = standard deviation, n = number, % = percentage

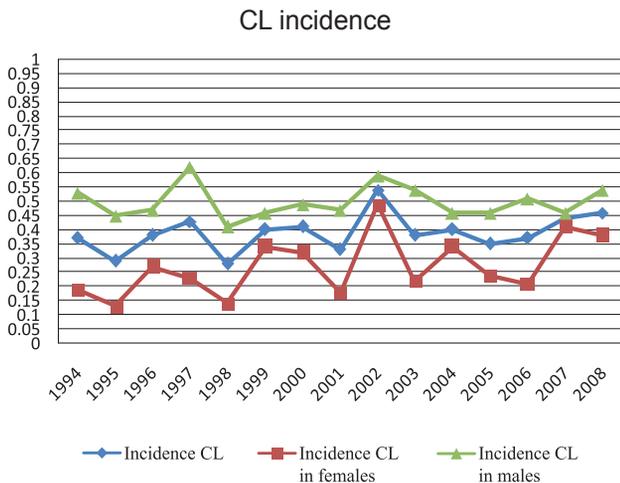
**Tab. 2. Gender differences in cleft subgroups between years 1994–2008 - absolute numbers, percentage, incidence per 1000 live births, ratio per live births (one in all live births) and sex ratio male to female and female to male.**

Type	Gender	n	%	Incidence per 1000 live births	Ratio per live births	Sex ratio
CL	M	376	65.6%	0.5 ( $\sigma$ 0.06)	1/2037	2.07
	F	197	44.4%	0.27 ( $\sigma$ 0.01)	1/4226	0.55
CLP	M	554	65.8%	0.73 ( $\sigma$ 0.14)	1/1439	1.85
	F	288	44.2%	0.41 ( $\sigma$ 0.08)	1/2564	0.58
CP	M	492	49.1%	0.64 ( $\sigma$ 0.14)	1/1630	0.92
	F	510	50.9%	0.71 ( $\sigma$ 0.1)	1/1433	1.15
CL/P	M	1422	59%	1.87 ( $\sigma$ 0.27)	1/547	1.37
	F	995	41%	1.39 ( $\sigma$ 0.19)	1/733	0.76

CL = cleft lip, CLP = cleft lip and palate, CP = cleft palate, M = male, F = female, CL/P = cleft lip and/or palate,  $\sigma$  = standard deviation, n = number, % = percentage



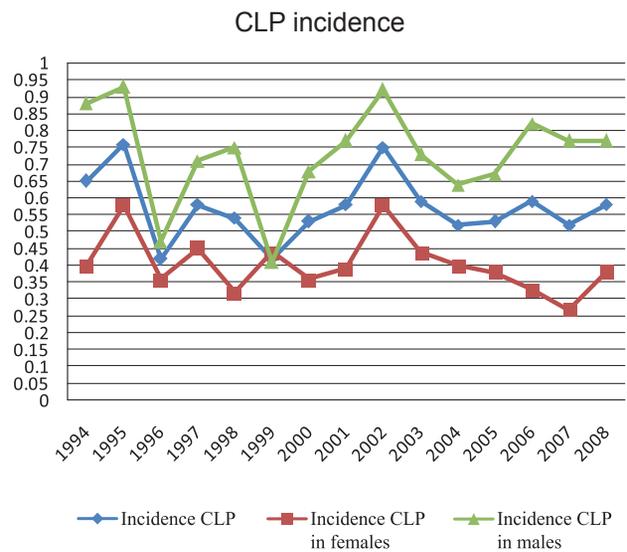
**Fig. 1. Development of the incidence of the CL/P between years 1994 and 2008 for both genders and for males and females separately.**



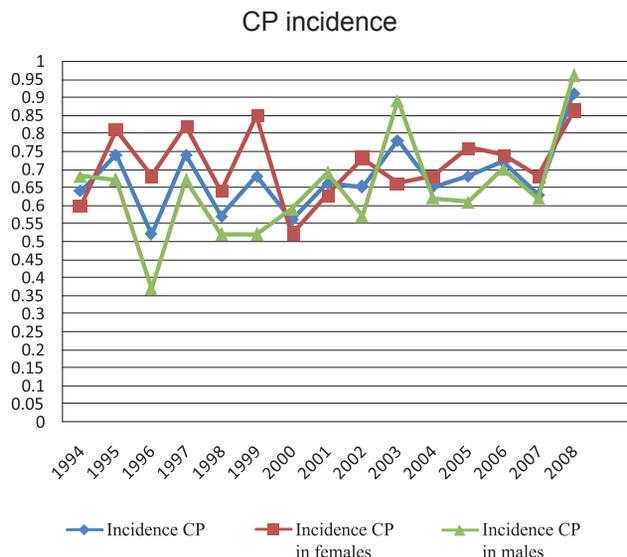
**Fig. 2. Development of the incidence of the CL between years 1994 and 2008 for both genders and for males and females separately.**

able trend (Fig. 1). Among all cleft cases, there were 573 cleft lip patients, 842 cleft lip and palate and 1002 cleft palate patients. The incidence of cleft lip was 0.39/1000 ( $\sigma$  0.07), the incidence of cleft lip and palate was 0.57/1000 ( $\sigma$  0.1) and 0.68/1000 ( $\sigma$  0.1) in cleft palate patients (Tab. 1). The ratio per live births for cleft lip patients was 1/2648 (1/2037 in males, 1/4226 in females), for cleft lip and palate patients 1/1801 (1/1439 in males, 1/2564 in females) and 1/1505 for cleft palate patients (1/1630 in males, 1/1433 in females).

The sex ratio in new born cleft children was 1.47 with male predominance. Among the infants affected by an orofacial cleft, males represented 59 % and females 41 % (1422 males and 995 females). The incidence of male cleft newborns was constantly higher, except for the year 1996, when the incidence of both genders was equal and in the year 1999, when the incidence of females exceeded the incidence of males. In the whole time period, the incidence of the cleft lip was 0.5/1000 ( $\sigma$  0.06) in males and



**Fig. 3. Development of the incidence of the CLP between years 1994 and 2008 for both genders and for males and females separately.**



**Fig. 4. Development of the incidence of the CP between years 1994 and 2008 for both genders and for males and females separately.**

0.27/1000 ( $\sigma$  0.1) in females. The sex ratio in cleft lip patients was 2.07 in the time period studied. The cleft lip and palate incidence was 0.73/1000 ( $\sigma$  0.14) in males and 0.41/1000 ( $\sigma$  0.08) in females. The sex ratio was 1.85 in cleft lip and palate children. The incidence of cleft palate was 0.64/1000 ( $\sigma$  0.14) in males and 0.71/1000 ( $\sigma$  0.1) in females, the sex ratio being 0.92 (Tab. 2).

No traceable trend was found in any of the data series, distribution of the incidence each year was totally random (Figs 1–4). Coefficient of slope in regression line has not been found statistically significant at 0.05 significance level in any of the time series investigated (Tab. 3). The greatest variability in the data was found in the incidence of cleft lip and palate anomalies in females,

**Tab. 3. Results of the linear regression model for all cleft types.**

Cleft type	Estimate	p
CL/P	0.0125	0.26
CL/P M	0.0078	0.52
CL/P F	0.0166	0.32
CL	0.0058	0.15
CL M	0.0004	0.92
CL F	0.0117	0.06
CL	-0.0028	0.65
CL M	0.0015	0.87
CL F	-0.0070	0.18
CP	0.0090	0.12
CP M	0.0146	0.09
CP F	0.0038	0.54

Estimate – estimation of the coefficient of linear regression line, p – p-value, CL/P = cleft lip and/or palate, CL = cleft lip, CLP = cleft lip and palate, CP = cleft palate, M = male, F = female

where the values shifted more than two standard deviations in the years 1995 and 2002.

### Discussion

Orofacial clefts are the most frequent congenital malformations of head and neck. The complex medical, ancillary and psychosocial interactions necessary in the management of a patient with cleft warrants a multidisciplinary team approach (35–36). Monitoring of the long-term incidence of orofacial clefts is of great importance to determine needs for future treatment in the National Health Service.

In the current study, the cleft incidence in the Czech Republic during 1994–2008 was 1.64 per 1000 live born infants. The incidence of CL/P in the former Czechoslovakia reported by Grundlach and Maus (19) ranged from 0.85 to 2.0 per 1000 live born infants the data were extracted from scientific references published between 1960 and 2000. Our results are almost in the middle of this range, slightly closer to the higher limit than to the lower. However, we still have to consider the differences in the populations sampled. In our study only the population of the Czech Republic, and not the larger population of the whole Czechoslovakia, was taken into account. The long term results of the incidence of CL/P in the region of the Czech Republic were published by Peterka et al (18) and earlier by Cerny et al. (17). Cerny and co-workers reported the occurrence of CL/P 2 per 1000 live births among the Czech population for the 1964–1983 period. In recent years, the ratio per live births was 1 per 600 live births so the number of cleft patients was lower than in the research done by Cerny et al in the time period studied. This may be because in the former sample also some syndromic clefts and atypical clefts were included. Peterka in his study mapped the incidence of CL/P in Bohemia in years 1964 to 1992. The mean incidence reported in the study was 1.74 per 1000 live born infants (18). Bohemia is a region of the Czech Republic, so the patient sample from Peterka's study did not include patients from Moravia and Silesia. Our results are lower than those presented by Peterka – the shorter time period studied or the missing data from Moravia and Silesia could account for the difference in the incidence, because the incidence differs slightly in every region of the Czech Republic (37).

The results of this study can usefully be compared to with the study from Slovak Republic, where the data about CL/P patients were gathered between 1985–2000. Machacova et al (38) presented a study where the clinical data of children with CL/P examined and operated on in the three main specialized departments of plastic surgery in the Slovak Republic over 16 years were collected. In contrast with the current study, in the Machacova's study the patients sample included cleft patients handicapped with additional malformations. Compared to the current study, this study revealed a slightly lower incidence of 1.61 per 1000 live born infants.

The incidence of CL/P in the current study differed from year to year with a greater or lesser variance with no traceable trend. The aetiology of these deviations is not clear – some authors believe that maternal exposure to viral infections and teratogens on population level have to be blamed (16). According to Peterka's findings, the incidence of CL/P during 29 years (from 1964 to 1992) was quite stable, with the annual incidences ranging between the minimal and maximal values 1.46/1000 and 2.28/1000 respectively (18). The values did not differ significantly from the mean incidence, with exception of the year 1985. In 1985, the incidence of CL/P rose to 2.28/1000 and both males and females contributed to this rise. The explanation of authors of the study is that this rise might be caused by some unknown exogenous harmful factor. On the other hand, in the report from the Slovak Republic, the lowest incidence was observed in 1985 (1.19/1000) and the highest in 1994 (2.09/1000) (38). A significantly higher incidence than average was reported also in year 1992 (2.01/1000). These higher rates of incidence were explained by the authors as being caused by higher morbidity rates of acute respiratory diseases in the first months of these years. In our study, we found the highest incidence in the year 2003 (2.13/1000), the second highest in the year 2008 (1.95/1000) and the lowest incidence in the year 1996 (1.32/1000). The inter-year variations in the incidence of the CL/P were totally unpredictable with no traceable trend, the same was found in previous studies (18, 38–39). Because of these unexplained variations in the incidence, further monitoring of the new born infants with CL/P is necessary in order to identify the specific environmental teratogen causing the increase of the anomaly.

Similarly, as in other studies, sexual differences were found in the incidence of CL/P. The anomaly was more frequent in males than in females. In our sample, out of all patients affected by a CL/P in years 1994–2008, there were 59 % boys and 41 % girls. This is in accordance with previous studies - the proportion of the affected boys and girls in the Bohemian sample in the years 1964–1992 was 57 % to 43 % (18, 40). The sex ratio stated for the Slovak Republic for the years 1985–2000 was 1.14 with male predominance (38). The sex ratio differs also between clefts of primary and secondary palate. The male to female ratio in our sample was 2.07 in the cleft lip patients and 1.85 in cleft lip and palate patients. The higher incidence of cleft lip and cleft lip and palate in boys might be caused by a higher sensitivity of male foetuses to environmental stress leading to the appearance of congenital birth defects (41). Also, perinatal mortality is higher in males across the whole range of gestational age (42). Strong external stimulus causes spontaneous abortion preferentially in male foetuses. Look-

ing to our results, we can explain the drop in incidence of male cleft infants in years 1996 and 1999 by an exogenous harmful factor which led to extensive infliction of male fetuses leading to abortions of most of the male embryos affected.

In cleft palate patients, the male to female ratio was lower at 0.92 with predominance in girls, results compatible with previous studies (17–18, 38–39, 43–44). The possible explanation of this fact may be in gender differences in the development. The cleft palate can result from an abnormality in palatogenesis itself, e.g. by mutations in genes involved in fibroblast growth factors, hedgehog and bone morphogenetic protein signalling, or it can be caused by effects of the abnormalities in development or function of tongue, mandible or cranial base (5, 35). Gene mutations are not affected by gender of the foetus, but there are some differences in the intrauterine orofacial development in boys and girls. Craniofacial growth progressively displaces the tongue downward and forward in the oral cavity, thus allowing space for palatal shelves to relocate above the tongue. During these stages of facial development, there is almost no growth in head length. In females, the palatal shelves elevate in the 8th gestational week while this takes place in the 7th week in male fetuses. The shelves are less likely to come into close anatomical contact in a continually growing craniofacial complex. This may contribute to the predominance of cleft palate in girls (5). However, to understand the exact cause of this phenomenon, further epidemiological studies are necessary.

Looking at the incidence of the three cleft groups separately, isolated cleft palate is the most common type of cleft in the Czech Republic with the highest incidence among all other orofacial clefts. This is in accordance with other studies (17–18, 38, 44). Evaluating just two groups of cleft anomalies – CL+CLP and separate CP, incidence of cleft lip with or without cleft palate is higher, or in absolute terms 1415 CL+CLP patients to 1002 CP patients.

CL/P are common birth defects that vary in incidence according to the ethnicity and geographic origin, with populations of Asians having the highest rates and African ancestry the lowest (2–3, 44–48). In the Czech Republic, the proportion of ethnical minorities is very small, 96 % of the inhabitants are Caucasians (49). The reported incidence of CL/P in Caucasian population varies from 0.69 to 2.35 per 1000 live born infants in the study published by Grundlach and Maus (19). The study of birth incidence in Scotland in years 1971–1990 showed an occurrence 1.4/1000. In Finland, the total incidence in 1967–1971 was 1.71/1000 and in Denmark in 1988–2001 it was 1.44 per 1000 live born infants (19, 39, 50–51). Thus, we can say that the results presented in this study are consistent with previous studies on populations with a very high proportion of Caucasians.

Further long-term studies are necessary in order to elucidate the exact causes of cleft anomalies, the long-term trends and oscillations in incidence of craniofacial clefts in the Czech Republic. Identifying the probable environmental teratogen may decrease the incidence of cleft anomalies in the future. The data gathered about the progress of the incidence give a starting indication for planning health service resource requirements for this group of affected infants.

## Conclusions

The incidence of nonsyndromic CL/P in the Czech Republic in 1994–2008 was 1.64 per 1000 live born infants or one in 600 live births. This is close to the incidence reported in previous studies performed in central Europe and on Caucasian ancestry.

The incidence of nonsyndromic CL/P in the Czech Republic exhibited neither increasing nor decreasing tendency between years 1994–2008.

Isolated cleft lip and cleft lip and palate are more frequent in males. In the case of cleft palate, the incidence in females is slightly higher than in males.

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Received June 1, 2011.

Accepted November 30, 2011.