European Journal of Medical Genetics 61 (2018) 489–492

Contents lists available at ScienceDirect

European Journal of Medical Genetics

journal homepage: www.elsevier.com/locate/ejmg

Epidemiology of orofacial clefts in a Danish county over 35 years – Before and after implementation of a prenatal screening programme for congenital anomalies

Eva Berenth Paaske[a], Ester Garne[b,*]

[a] Department of Anesthesiology and Intensive Care, Odense University Hospital, Denmark
[b] Paediatric Department, Hospital Lillebaelt - Kolding, Denmark

ARTICLE INFO

Keywords:
Population-based
Cleft lip with or without cleft palate
Cleft palate
Prevalence
Orofacial clefts
Prenatal diagnosis

ABSTRACT

In 2004 the Danish National Board of Health changed its screening recommendations. Since 2005 a first trimester screening for Down syndrome and a prenatal ultrasound screening for congenital anomalies in the second trimester of pregnancy has been offered to all pregnant women.

The aim of this study was to describe the prevalence of cleft lip with or without cleft palate and cleft palate in a Danish area and to describe associated anomalies and the development in prenatal diagnosis over time. The study was based on data from the EUROCAT Registry for Funen County. The registry is based on multiple data sources and includes information about live births, fetal deaths with a gestational age > 20 weeks and terminations of pregnancy after prenatal diagnosis of severe fetal anomaly. The study included all fetuses/infants out of a population of 182,907 births diagnosed with orofacial clefts born between 1980 and 2014. There were 271 cases diagnosed with cleft lip with or without cleft palate and 127 cases diagnosed with cleft palate, giving a prevalence of 14.8 per 10,000 births for cleft lip with or without cleft palate and 6.9 per 10,000 births for cleft palate. There were no significant changes in prevalence over time for the two anomalies, calculated with and without inclusion of genetic and chromosomal cases. Overall 66 cases were diagnosed prenatally (17% of total). For isolated cleft lip with or without cleft palate none of the 157 cases born before 2005 were diagnosed prenatally compared to 34 of 58 cases (59%) born in 2005–2014 ($p < 0.01$). The proportion of liveborn infants with multiple congenital anomalies also changed after 2005 with 15% (39/266) of all liveborn infants with orofacial clefts born 1980–2004 having multiple anomalies compared to 7% (7/96) in 2005–2014 ($p < 0.05$).

The implementation of the new screening programme in 2005 has given a major change in prenatal detection rate and reduced the proportion of liveborn infants with orofacial clefts classified as multiple congenital anomaly cases. The prevalence of cleft lip with or without cleft palate was higher than reported from many other countries.

1. Introduction

Cleft lip with or without cleft palate (CLP) and cleft palate (CP) can arise as an isolated malformation or in association with other anomalies or be a part of a syndrome. The most frequent is the isolated cleft which epidemiological and family studies have suggested are due to both environmental and genetic factors (Bille et al., 2005; Christensen et al., 1992). CLP are easily diagnosed at birth, while CP may be diagnosed days or weeks after birth. CLP and CP can be surgically corrected with satisfying cosmetic result (Christensen, 1999). However, both anomalies have significant psychological and socio-economic effects on patient quality of life and require a multidisciplinary team approach for management (Shkoukani et al., 2013; Sischo et al., 2017).

In 2011 a large international study (IPDTOC, 2011), including data from 54 registries around the world, analyzed the prevalence at birth of CLP into 11 areas according to their geographical location: Canada, United States, Mexico and South America, British Isles, Western Europe, Eastern Europe, South-Mediterranean Europe, United Arab Emirates, South Africa, Japan, and Australia. The overall prevalence of CLP was 9.92 per 10,000 births with significant differences around the world. The lowest prevalences were registered in South Africa, Italy, and US, whereas the highest reported prevalences were in Japan, Germany and Denmark.

A European study on CP showed an overall prevalence of cleft palate

* Corresponding author. Paediatric Department, Hospital Lillebaelt, DK – 6000, Kolding, Denmark.
E-mail address: Ester.garne@rsyd.dk (E. Garne).

https://doi.org/10.1016/j.ejmg.2018.05.016
Received 24 February 2018; Received in revised form 2 April 2018; Accepted 8 May 2018

at 6.2 per 10,000 births with less geographical variation in prevalence than for CLP, except for a very high rate of cleft palate in Finland (Calzolari et al., 2004). CP was often associated with other major congenital anomalies (1740 of 3852 cases; 45.2%).

Prenatal screening for congenital anomalies is performed in most European countries (Boyd et al., 2008). In Denmark, prenatal screening using invasive testing for Down syndrome was offered for advanced maternal age until 2004. In the same period prenatal ultrasound examinations were performed for specific indications only. In 2004 the Danish National Board of Health changed its screening recommendations. Since 2005 a first trimester screening for Down syndrome and a prenatal ultrasound screening for congenital anomalies at gestational age 18–20 weeks r of pregnancy has been offered to all pregnant women (Sundhedsstyrelsen, 2017).

The aim of this study is to describe the prevalence of CLP and CP in a Danish area and to describe associated anomalies and the development in prenatal diagnosis over time.

2. Material and methods

The European Surveillance of Congenital Anomalies (EUROCAT) is a network of population-based congenital anomaly registries in Europe, with the central registry funded by the European Union. It has been in operation for more than 35 years and it currently surveys more than 1.7 million births per year by 43 registries in 23 countries. The EUROCAT databases contain data collected routinely, using multiple data sources, on all major congenital structural and chromosomal anomalies.

This study is based on data from the EUROCAT registry for Funen County. The study population included all fetuses/infants born with a diagnosis of a facial cleft in 1980–2014, where the mother was resident in Funen County at the time of birth or abortion among 182,907 births (live and stillbirths) during the 35 years. The EUROCAT registry of Funen County is population-based and uses standardized methods of case ascertainment (Boyd et al., 2011). The registry is based on multiple data sources including hospital records, birth and death certificates, annual reports from the cytogenetic laboratory and post-mortem examinations. The individuals included in the registry are live births (LB) diagnosed at birth or within the first five years after birth, fetal deaths (FD) with a gestational age (GA) of 20 weeks or more, and terminations of pregnancy (TOPFA) at any GA after prenatal diagnosis of a major fetal anomaly. All structural malformations, syndromes and chromosome anomalies are included in the database, except for minor and poorly specified malformations when isolated found on an exclusion list (EUROCAT, 2016, Froslev-Friis et al., 2011). Each case can have up to 9 diagnoses (one syndrome variable and 8 variables for malformations) and are coded by a pediatrician after review of the medical records. The coding system was ICD9 up to 1999 and from 2000 ICD10 was used, both with the British Pediatric Extension (EUROCAT, 2016). Cases were classified as isolated or multiple congenital anomalies according to the EUROCAT algorithm for case classification (Garne et al., 2011). In EUROCAT a case is defined as diagnosed prenatally if one anomaly is diagnosed before birth. Therefore, for multiple congenital anomaly cases it is not recorded which anomalies were diagnosed prenatally and which were diagnosed after birth or at termination.

Statistical Methods: Descriptive data are presented with percentages. The Chi-square test was used for comparison of groups. Trends of the prevalence over time were calculated using Poisson regression in single years, and these were plotted in five year groups (1980–84; 1985–89; 1990–94; 1995–99; 2000–04; 2005–09; 2010–14).

The 95% confidence intervals were calculated using the Poisson approximation.

3. Results

The study included 398 total cases with orofacial clefts: 271 cases diagnosed with CLP and 127 cases diagnosed with CP, giving a prevalence of 14.8 per 10,000 births for CLP and 6.9 per 10,000 births for CP. The total prevalence over time in 5-year intervals is presented in Fig. 1. There were no significant changes in prevalence over time for the two anomalies, calculated with and without inclusion of genetic and chromosomal cases. The incidence rate ratio per ten years was 0.96 (95%CI: 0.85–1.08) for CLP and 0.99 (95%CI: 0.83–1.19) for CP.

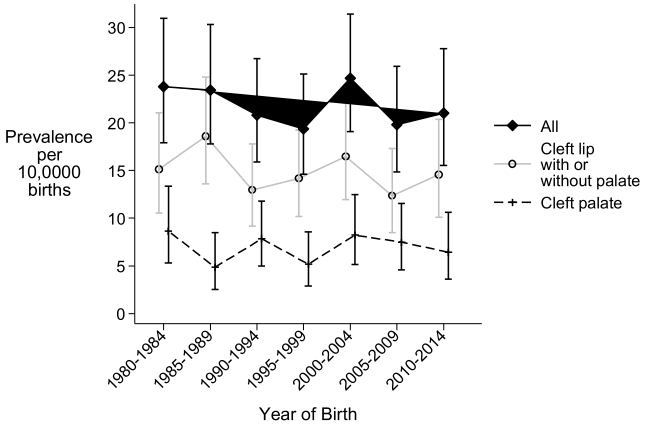

Fig. 1. Total prevalence of orofacial clefts, Funen County 1980–2014.

The majority of cases were liveborn infants (91%) and 4.5% were fetal deaths from 20 weeks of gestation and 4.5% were TOPFA (Table 1). There were no TOPFA with isolated orofacial cleft.

Table 2 shows the EUROCAT classification of all 398 cases from 1980 to 2014. For CLP 215 cases (79%) were classified as isolated anomaly and for CP 78 (61%) were classified as isolated ($p < 0.05$). Multiple congenital anomalies were present in 34 cases with CLP (13%) and in 27 cases (21%) with CP ($p < 0.05$). The most frequent associated anomalies were limb defects, congenital heart defects, cerebral anomalies and eye anomalies. Among the 271 cases with CLP 161 (59%) had cleft palate.

Overall 66 (17%) of all orofacial cleft cases were diagnosed prenatally. The time of diagnosis in the years 1980–2004 compared to 2005–2014 is presented in Table 3. There was a statistically significant increase in the proportion of cases diagnosed prenatally ($p < 0.001$). The increase was related to the prenatal diagnosis of CLP as the proportion of prenatal diagnosis of CP did not change. For isolated CLP none of the 157 cases born before 2005 were diagnosed prenatally compared to 34 of 58 cases (59%) born in 2005–2014. No cases with isolated CP were diagnosed prenatally. The proportion of liveborn

Table 1
Prevalence of orofacial clefts in Funen, Denmark, 1980–2014 based on EUROCAT data and a population of 182,907 births.

	1980–2014
Total facial clefts	398
Rate per 10,000 births	21.8 (95% CI: 19.6–24.0)
Terminations of pregnancy for fetal anomaly	18 (4.5%)
Fetal deaths from GA[a] 20 weeks	18 (4.5%)
Livebirths (% of total)	362 (91%)
Cleft lip with/without cleft palate	
Total cases	271
Rate per 10,000 births	14.8 (95% CI: 13.1–16.7)
Terminations of pregnancy for fetal anomaly	13 (5%)
Fetal deaths from GA[a] 20 weeks	14 (5%)
Livebirths (% of total)	244 (90%)
Cleft palate	
Total cases	127
Rate per 10,000 births	6.9 (95%CI:5.8–8.3)
Terminations of pregnancy for fetal anomaly	4 (3%)
Fetal deaths from GA[a] 20 weeks	5 (4%)
Livebirths (% of total)	118 (93%)

[a] GA = gestational age.