Cleft Lip and Palate among Hispanics in California

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The goal of this study was to determine the epidemiological characteristics of orofacial clefts [cleft lip (CL), cleft palate (CP), cleft lip and palate (CLP), and "atypical" clefts] and conditions in which they occur among Hispanics. We analyzed a population-based sample of 4,433 cases ascertained from 2,509,881 California births. Out of these 1,595 (35.98%) were ascertained from 923,578 Hispanic California births during the 11 year period 1983-1993. We classified all cases according to our previously introduced classification: isolated cleft anomalies, sequences of the primary defect, chromosomal aberrations, monogenic syndromes, results of known teratogens, associations, multiple congenital anomalies (MCA) of unknown etiology, or conjoined twins. The birth prevalence of isolated CL±P was 0.74 per 1,000 births (CL 0.22/ 1,000, CLP 0.53/1,000), of isolated CP 0.23 per 1,000 births, and of Robin sequence 0.04 per 1,000 births. No significant differences were found when prevalences of isolated orofacial clefts were calculated for the subgroup of children of Hispanic mothers who were born in Mexico and then moved to California. Isolated anomalies constituted 57.05% of clefts. In the total sample, there were 3.89% sequences, 9.54% chromosomal aberrations, 6.08% monogenic syndromes, 1.25% associations, 22.13% of MCA of unknown etiology, and 0.06% in conjoined twins. The usual predominance of males was found in CL and CLP cases in both subgroups -isolated and multiples [male:female ratio=1.64 (CL, CL/MCA); 1.79 (CLP); 1.71(CLP/MCA)]. In CP only, the usual predominance of females was found (male:female ratio=0.76). Among CP/MCA, a predominance of males was found (male:female ratio=0.92). Evaluation of the sample by maternal age groups revealed the highest risk for having a baby affected with isolated CL±P to be 20-24 years. The highest risk for having a baby affected with isolated CP was found in mothers younger than 20 years. The risk for having a baby affected with C/MCA was highest for CLP in the subgroup of mothers 35 years old and older and with CP/MCA in mothers younger than 20 years. This study presents essential information regarding the epidemiology of orofacial clefts in the Hispanic population in California, and provides a framework for genetic counseling and other studies focused on causes and prevention of these serious anomalies.

Introduction

Orofacial clefts ["typical"cleft lip (CL), Figures 1, 2; cleft lip and palate (CLP), Figures 3, 4, 5, 6 and 7; cleft palate only (CP), Figures 8 and 9], and "atypical" clefts, Figure 10] occur either as isolated anomalies or together with other congenital anomalies [multiple congenital anomalies (MCA)]. They are among the most common birth defects, affecting approximately one baby in 550 newborns worldwide. Almost every hour in the United States (U.S.), a baby with orofacial cleft is born and 7,500 are born with cleft in the U.S. every year. The estimated average lifetime medical cost is $100,000 per affected child,[1] amounting to $750 million for all such children born in one year's time. Orofacial clefts represent an etiologically heterogeneous group of congenital anomalies, therefore the correct diagnosis of a cleft anomaly is fundamental for any further genetic and etiopathological studies as well as for preventive measures, targeting correctly the class of orofacial clefts that are preventable.

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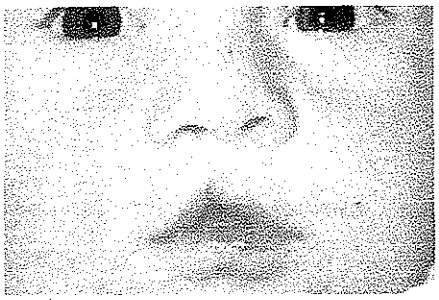

Figure 1. Unilateral cleft lip on the left side.

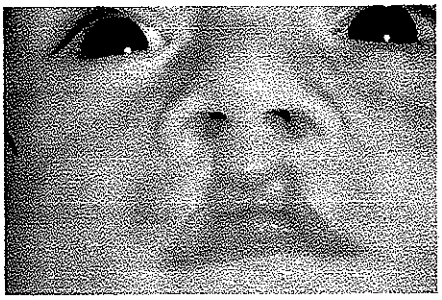

Figure 2. Bilateral cleft lip.

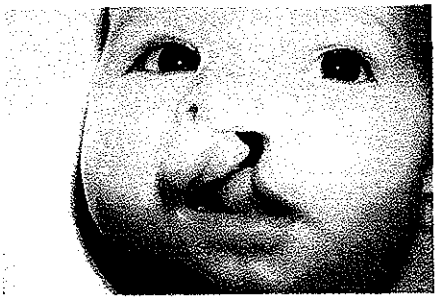

Figure 3. Unilateral cleft lip and palate on the right side.

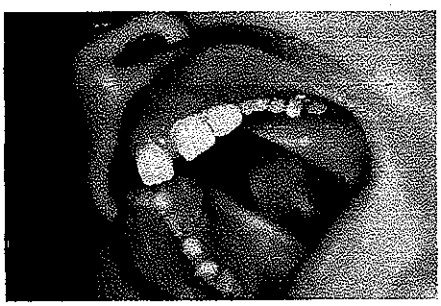

Figure 4. Unilateral cleft lip and palate - oral view.

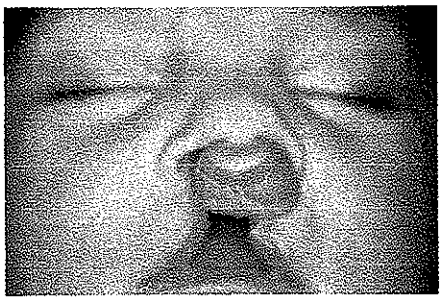

Figure 5. Bilateral cleft lip and palate.

Figure 6. Bilateral cleft lip and palate - lateral view.

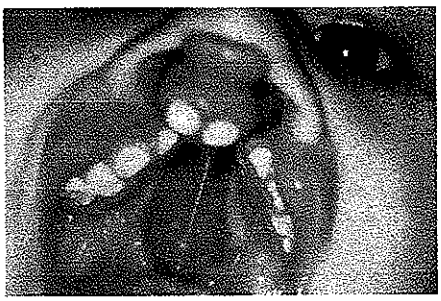

Figure 7. Bilateral cleft lip and palate - oral view.

Figure 8. Cleft palate.

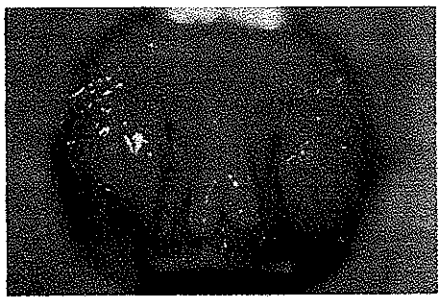

Figure 9. Cleft uvula.

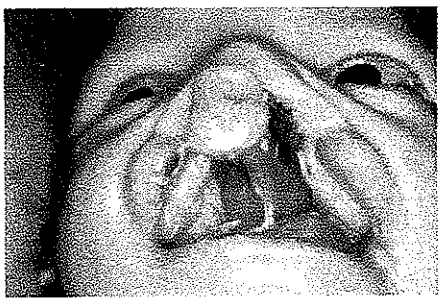

Figure 10. Bilateral cleft lip and palate combined with transversal (atypical) cleft on the left side.

With rapidly progressing new DNA diagnostic technologies, more and more cases of orofacial clefts are identified as syndromic. Thus, although the basic rate of clefting (1:500-550) has not changed since Fogh-Andersen[2] did his pioneering genetic study in 1942, we can now diagnose these clefts more accurately. In our present study we used our classification scheme of orofacial clefts,[3] which includes classification of MCA developed for the study of multiple congenital anomalies in the California population.[4,5]

It has been well recognized that there is a considerable difference in the incidence of clefts in different racial groups, the lowest being found in Blacks,[6,7] high in Japanese,[8] and the highest in North American Indian populations.[9,10] However, there were many weaknesses in previous studies (such as small sample size, data from birth certificates only, surgical samples, data from registries that were not "cleaned", etc.) which led to extreme differences in rates and to other biases.

A diverse multiracial population in California offers a singular opportunity to analyze large samples of congenital defects in major ethnic groups. In the present study, we focused our interest on the Hispanic population representing after non-Hispanic Whites the second largest ethnic group in the state. The large and unique population-based sample of 4,433 cases of orofacial clefts ascertained from 2,509,881 California births during an 11 year period (1983-1993),[3] allowed us to analyze a sample of 1,595 cases in 923,578 Hispanic

California births (36.8%). In this paper, we present an evaluation of the birth prevalence, sex distribution, and maternal age for isolated clefts and multiple cleft anomalies.

Material and methods

The sample consisted of 1,595 cases with any type of isolated or multiple orofacial cleft anomaly registered by the California Birth Defects Monitoring Program (CBDMP) registry from 1983 through 1993 who were born to Hispanic mothers. In agreement with ethnic composition of the state, this sample represents the second largest ethnic subgroup in our sample of 4,443 cases of orofacial clefts in our previous study.[3] The CBDMP registry is a regional population-based registry of congenital anomalies currently based on approximately 300,000 annual births.[11] CBDMP staff visits all hospitals and outpatient genetic centers in California counties to abstract data about all children with congenital anomalies diagnosed up to the age of 1 year. For each

Table 1. Orofacial clefts among Californian Hispanics. (Total births 923,578; years1983-1993)

Group	Type of anomaly	Type of cleft				TOTAL	
		CL	CLP	CP	Atypical	No.	%
1. Isolated anomaly (n=910, 57.05%)	Cleft lip (CL)	203	-	-	-	203	12.73
	Cleft lip and palate (CLP)	-	485	-	-	485	30.40
	Cleft palate (CP)	-	215	-	-	215	13.48
	Atypical facial cleft	-	-	-	7	7	0.44
2. Sequence (n= 62, 3.89%)	Robin sequence	-	-	39	-	39	2.45
	Holoprosencephaly sequence	1	4	3	12	20	1.25
	Frontonasal dysplasia sequence	-	-	1	1	2	0.13
	Amyoplasia cong. disruption sequence	-	-	1	-	1	0.06
3. Chromosomal aberrations (n=152, 9.54%)	Trisomy 21	-	1	6	1	8	0.50
	Trisomy 13	-	31	14	5	50	3.13
	Trisomy 18	2	19	9	-	30	1.88
	Other trisomies	1	3	6	-	10	0.64
	Other chromosomal aberrations	4	24	24	2	54	3.39
4. Monogenic syndromes (n=97, 6.08%)	Autosomal dominant (AD)	2	14	45	8	69	4.32
	Autosomal recessive (AR)	1	4	15	1	21	1.32
	X-Linked dominant	-	-	2	-	2	0.13
	Mostly sporadic but also AD or AR	-	-	5	-	5	0.31
5. Known environmental cause (n=0)		-	-	-	-	-	-
6. Associations (n=20, 1.25%)		2	10	8	-	20	1.25
7. Multiple congenital anomalies (MCA) of unknown etiology (n=352, 22.07%)	MCA of malformation origin	18	114	98	21	251	15.73
	MCA of deformation origin	-	-	1	-	1	0.06
	MCA of malformation and deformation origin	4	18	36	4	62	3.89
	MCA of disruption origin	2	4	5	1	12	0.75
	MCA of disruption and malformation origin	4	13	7	2	26	1.64
8. MCA of other combinations (n=1, 0.06 %)		-	-	1	-	1	0.06
9. Conjoined twins (n=1, 0.06 %)		-	1	-	-	1	0.06
TOTAL (n=1,595, 100 %)		244	745	541	65	1,595	100.00

specific diagnosed anomaly, CBDMP staff members record: 1) the type of physical examination and/or medical procedure and/or confirmatory test used to establish the diagnosis, and 2) the subspecialty of the physician who made the diagnosis. Data from 1983 through 1993 yielded a total of 923,578 births to Hispanic mothers, of which 917,648 were live births and 5,930 stillbirths. Abstracts of all registered cases (n=1,595) were reviewed by an author (medical geneticist) and cases were classified according to the system previously published.[3,4,5] For clarification of the diagnosis, additional information was obtained from medical facilities.

We calculated the percentage of newborns with orofacial clefts who had an isolated anomaly and the percentage with any other condition in which orofacial clefting was involved. We calculated the birth prevalence of clefts per 1,000 births for each subgroup of isolated as well as multiple cases, for subgroups of Mexican-born mothers, and for maternal age subgroups. The 95% upper and lower confidence intervals (CIs) based on the Poisson distribution were calculated for each estimate and for the overall estimate.

Figure 11. Robin sequence.

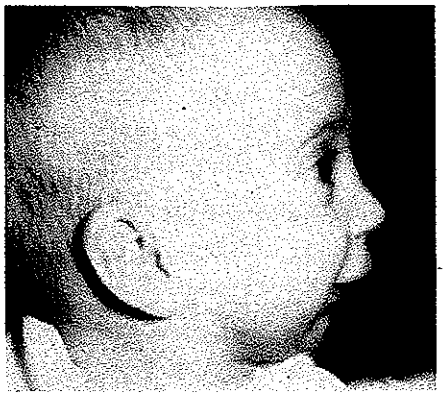

Figure 12. Robin sequence - lateral view.

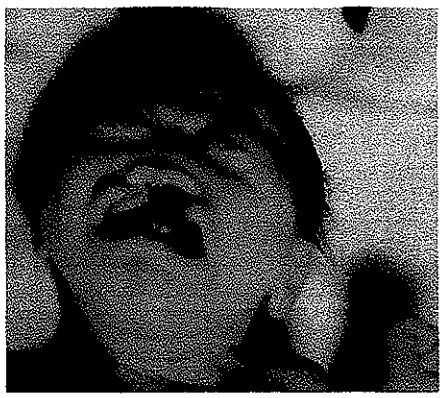

Figure 13. Holoprosencephaly sequence with missing premaxila in large median (atypical) cleft.

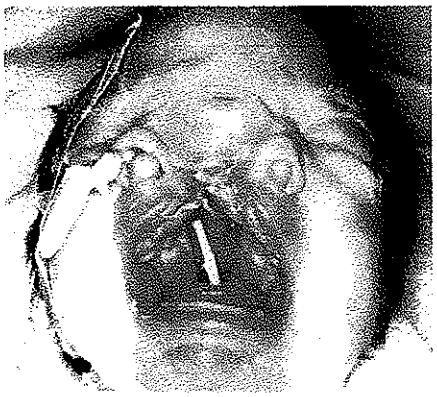

Figure 14. Frontonasal dysplasia sequence.

Results

All 1,595 cases in our sample were classified into one of 9 major groups. Within each major group, subclassification was done according to final individual diagnoses (for groups 1 through 6) or according to the best estimate of etiological origin (for group 7). Cases were identified as all live born or stillborn (>20 weeks of gestation) infants affected with an orofacial cleft and diagnosed up to 1 year of age.

Types of Orofacial Clefts

In our sample of 1,595 cases of orofacial clefts, only 57.05% occurred as isolated anomalies (Table 1). The largest proportion of isolated clefts –75.6%– were cleft lip with or without cleft palate (CL±P), of which 70.5% were CLP. Isolated atypical clefts were diagnosed in 7 cases. Sequences were found in 3.89%, and the remaining 39.06 % were cases other than isolated or sequences. The group of sequences consisted mostly of two sequences: Robin sequence [(n=39), Figures 11 and 12] and holoprosencephaly sequence [(n=20), Figure13]. There were two cases of frontonasal dysplasia sequence (Figure14) and one case of amyoplasia congenita disruption sequence. Clefts in chromosomal aberrations were obser-ved in 152 cases (9.54%). The most frequent unique diagnosis was trisomy 13 (n=50), followed by trisomy 18 (n=30). Among 97 cases (6.08%) of monogenic syndromes, the most frequent were autosomal dominant syndromes (n=69). There were 20 cases in which orofacial clefts occurred in known association. The largest proportion of nonisolated nonsequence cases (56.5%) were multiple congenital anomalies of unknown etiology (n=352). In the vast majority of cases (n=251; 71.3%), MCA were of a malformation origin. The second largest group consisted of MCA of a malformation and deformation origin (n=62).

Birth Prevalence

The overall prevalence of any kind of orofacial cleft was 1.73 per 1,000 total births (live births and stillbirths), indicating that one case of isolated cleft or multiple cleft anomalies occurred in approximately every 580 births.

The birth prevalence of isolated CL±P was 0.74 per 1,000 births (1:1,340). When the prevalence was evaluated separately for CL and CLP, the rate for CL was 0.22 per 1,000 births (1:4,550) and for CLP 0.53 per 1,000 births (1:1,900). For isolated CP, the prevalence was 0.23 per 1,000 births (1:4,300) (Table 2.). Isolated atypical clefts were diagnosed in seven cases, with a birth prevalence of 0.008 per 1,000 births.

Table 2. Prevalence of nonsyndromic, nonmultiple orofacial clefts, Robin sequence and clefts in holoprosencephaly sequence in 923,578 Hispanic California births (years 1983-1993).

Type of cleft	Prevalence per 1,000 births		
	No.	Rate	95% CI
Cleft lip (CL)	203	0.22	0.19, 0.25
Cleft lip and palate (CLP)	485	0.53	0.48, 0.57
Cleft lip with or without cleft palate (CL±P)	688	0.74	0.69, 0.80
Cleft palate only (CP)	215	0.23	0.20, 0.27
Atypical facial cleft	7	0.008	0.003, 0.016
Robin sequence	39	0.04	0.03, 0.06
Orofacial cleft in holoprosencephaly sequence *	15	0.02	0.01, 0.03

* Included only cases of holoprosencephaly sequence without major anomaly (unrelated to the sequence) and with normal or unknown karyotype

Table 3. Prevalence of isolated orofacial clefts in 517,181 total births of Mexican- born mothers (years 1983-1993).

Type of cleft	Prevalence per 1,000 births		
	No.	Rate	95% CI
Cleft lip (CL)	110	0.21	0.17, 0.26
Cleft lip and palate (CLP)	269	0.52	0.46, 0.59
Cleft lip with or without cleft palate (CL±P)	379	0.73	0.66, 0.81
Cleft palate only (CP)	121	0.23	0.19, 0.28

Table 4. Prevalence of nonsyndromic, nonchromosomal multiples with CL, CLP, CL±P, and CP in 923,578 Hispanic California births (years 1983-1993).

Type of cleft in MCA (C/MCA)	Prevalence per 1,000 births		
	No.	Rate	95% CI
Cleft lip in MCA (CL/MCA)	29	0.03	0.02, 0.05
Cleft lip and palate in MCA (CLP/MCA)	141	0.15	0.13, 0.18
Cleft lip with or without cleft palate in MCA (CL±P/MCA)	170	0.18	0.16, 0.21
Cleft palate in only in MCA (CP/MCA)	140	0.15	0.13, 0.18
Atypical facial cleft in MCA	29	0.03	0.02, 0.05

As expected, the most common sequence was the Robin sequence, which was diagnosed as an isolated, nonsyndromic condition in 39 cases with a birth prevalence of 0.04 per 1,000 births. Therefore, approximately 1 in every 6 to 7 nonsyndromic, nonchromosomal CP cases had Robin sequence. The second most common sequence was the holoprosencephaly sequence —cases with no other major anomaly related to the sequence and with normal or unknown karyotype— which was observed in 20 cases (prevalence 0.02 per 1,000 births).

Orofacial clefts in chromosomal aberrations (n=152) occurred with a birth prevalence of 0.16 per 1,000 births (CI=0.14,0.19). The most common was trisomy 13. Monogenic syndromes with orofacial clefts were found in 97 cases (0.11/1,000; CI=0.09,0.13). The most common were autosomal dominant syndromes (n=69; prevalence 0.07/1,000; CI=0.06,0.10). Known associations with orofacial clefts were observed in 20 cases (0.02/1,000;CI=0.01,0.03).

There were 352 cases of orofacial clefts with MCA of unknown etiology (C/MCA), for a prevalence of 0.38 per 1,000 births (CI=0.34,0.42). Orofacial clefts in MCA of a malformation and/or deformation origin constitute the majority of cases in this group (n=314; prevalence 0.34/1,000; CI=0.30,0.38). Remaining 38 C/MCA cases were of a malformation and/or disruption origin.

More than a half of the birth population in our sample (n=517,181; 56%) were infants of Hispanic mothers residing in California but born in Mexico. There were no significant differences found when prevalences of isolated orofacial clefts were calculated for the subgroup of infants of the Mexico-born Hispanic mothers (Table 3).

Among those cases of multiple congenital anomalies (MCA) of unknown etiology (i.e. nonsyndromic, nonchromosomal) where orofacial cleft occurred (C/MCA), the lowest prevalence was found for CL/MCA (0.03/1,000 births), the prevalence was and 5 times higher (0.15/1,000 births) for CLP/MCA and CP/MCA (Table 4).

Sex ratio

We found usual predominance of males in CL and CLP cases in both subgroups, isolated and multiples (Table 5). In CLP and CLP/MCA cases, the proportion of males was slightly higher compared to CL and CL/MCA cases (male:female ratios CL=1.64, CL/MCA=1.64; CLP=1.79, CLP/MCA=1.71). In CP only in isolated cases, the usual predominance of females was found (male:female ratio=0.76). Among CP/MCA, a predominance of males was found (sex ratio=1.33). A predominance of males was also found in cases of Robin sequence (sex ratio=1.17).

Maternal age

We calculated the birth prevalence of both isolated and multiple orofacial cleft anomalies separately for each of

Table 5. Sex ratio and prevalence of orofacial clefts among Hispanics in California by sex. (Hispanic California births: males 470,845, females 452,709; years 1983-1993).

Type of cleft			No.	Prevalence per 1,000 births Rate	95% CI	Male/Female ratio
Cleft lip (CL)	isolated	males	126	0.27	0.22, 0.32	1.64
		females	77	0.17	0.13, 0.21	
	MCA	males	18	0.02	0.01, 0.03	1.64
		females	11	0.01	0.01, 0.02	
Cleft lip and palate (CLP)	isolated	males	311	0.66	0.59, 0.74	1.79
		females	174	0.38	0.33, 0.45	
	MCA	males	89	0.10	0.78, 0.12	1.71
		females	52	0.06	0.04, 0.07	
Cleft palate only (CP)	isolated	males	93	0.20	0.16, 0.24	0.76
		females	122	0.27	0.22, 0.32	
	MCA	males	80	0.09	0.07, 011	1.33
		females	60	0.07	0.05, 0.08	
Atypical facial cleft	isolated	males	5	0.01	0.004, 0.026	2.50
		females	2	0.002	0.000, 0.008	
	MCA	males	13	0.03	0.02, 0.05	0.92
		females	16	0.04	0.02, 0.06	
Robin sequence		males	21	0.04	0.03, 0.07	1.17
		females	18	0.04	0.02, 0.06	

MCA = Nonsyndromic, nonchromosomal multiple congenital anomalies

the five maternal age groups: **1)** mothers younger than 20 years, **2)** mothers 20-24 years old, **3)** mothers 25-29 years old, **4)** mothers 30-34, and **5)** mother 35 years old and older.

The highest risk for having a baby with isolated CL or CLP [(Table 6.), Figure 15] was found for mothers 20-24 years old (CL: prevalence 0.26/1,000; CLP: prevalence 0.62/1,000). The lowest risk for CL was for mothers 30 years old and older (prevalence 0.17/1,000); for CLP, for those in age group 25-29 years (prevalence 0.44/1,000). The highest risk for having a baby affected with isolated CP was found in mothers younger than 20 years. The risk of having a baby affected with C/MCA [(Table 7), Figure 16] was highest for CLP in the subgroup of mothers 35 years old and older (0.22/1,000) and for CP/MCA again for the youngest mothers (0.19/1,000).

Discussion

Despite a large number of studies on cleft lip and palate anomalies in humans, only several publications are based on an analysis of other than European, U.S, and Japanese populations. Also, a majority of the studies are "hospital" based not population-based, with inherent flaws in epidemiological accuracy. Moreover, the variety of types of clefts, as well as the variety of conditions in which orofacial clefts occur, require detail classification. Both typical and atypical clefts may be syndromic or nonsyndromic or may occur in a complex of multiple anomalies. While this aspect is always considered when classification is done by geneticists[3,12,13,14,15] it is not always considered in other studies, especially those in which the congenital anomaly is ascertained at birth only. These factors make comparison of the prevalence and other epidemiological findings rather difficult.

In the present study we used the same classification of orofacial clefts (into 9 major etiological groups) introduced in our previous study.[3] Using this classification, isolated cases were found in 57.05% of all cases. For CL±P, isolated cases represented 70.1%. A higher proportion of isolated cases was found for CL as compared to CLP (83.6% and 65.6% respectively). For CP, isolated cases were found in 47.9%; for atypical clefts, in 30.8.8%. Jones,[2] evaluating a clinical sample of 428 patients with orofacial clefts and velopharyngeal insufficiency from the Cleft Palate Program in San Diego, found 71% of isolated cases with approximately the same proportions for CL±P and CP cases as in our study. Since a substantial proportion of

population is Hispanic in the San Diego area this is very probably true also for Jones' sample. Even if we consider that in the study by Jones,[12] an anomaly was considered an MCA when a cleft plus two additional major anomalies or cleft plus three additional minor anomalies occurred, and in our study, an anomaly was considered an MCA when cleft plus one major anomaly occurred, the proportions are in agreement.

Data reported on the prevalence of orofacial clefts vary according to the investigator, the country, and ascertainment.3 In general, in White populations, all types of typical orofacial clefts combined occur with a frequency of 1 per 500-550 live born children. There are few data available in the literature to compare the prevalence in Hispanic Whites. An overall prevalence reported for Mexico by the International Clearinghouse for Birth Defects Monitoring System (ICBDM, 1996)[16] was 1.63/1,000 (1.24/1,000 for CL±P and 0.39/1,000 for CP) for 1989-1993 and 1.64/1,000 for 1994. In the same report very low prevalence with very similar rates for CL±P and CP was reported from Spain: overall prevalence for 1989-1993 was 1.08/1,000 (CL±P= 0.56/1,000; CP=0.52/1,000) and for 1994 1.03/1,000 (CL±P=0.61/1,000; CP=0.42/1,000). In our study, the overall prevalence including atypical clefts was 1.73 per 1,000 births (1.66/1,000 without atypical clefts); the birth prevalence for isolated CL±P was 0.74/1,000 and for CP 0.22/1,000. If we calculate the prevalence combining isolated and multiple types, for CL±P it is 1.07/ 1.000 and for CP 0.59, which is lower compared to rates for Mexican population but higher compared to rates for Spain. Recently, Lopez-Camelo and Oriolo17 evaluated prevalence rates for 11 birth defects in Latin America for 13 geographic regions and found extreme differences in prevalence of CL±P. For example, birth prevalence for CL±P was in Altiplano (Bolivia) 2,55/1,000 births and in Peru 0.73/1,000 births.

A general discussion of the differences in prevalence was presented by Leck,[18] who combined 29 series from 19 countries. He concluded that most of the geographical variations of CL±P seem to be secondary to ethnic differences, however there is no doubt that the method of ascertainment and classification criteria have a major influence on prevalence values.

In our previous study,[3] when four major ethnic groups (non-Hispanic Whites, Hispanics, Asians and Blacks) were compared, the highest prevalence of all types of isolated clefts was found in non-Hispanic Whites: CL (0.34/ 1,000), CLP (0.47/1,000), CL±P (0.81/ 1,000), CP (0.35/1,000), and the lowest rates in Blacks (CL 0.19/1,000; CLP 0.22/1,000; CL±P 0.41/1,000 and CP 0.32/1,000). The rates for CL±P in Hispanics in this study (0.0.74/1,000) are lower compared to non-Hispanic Whites. The rate for CP (0.23/1,000) was the lowest compared to other racial groups and it was significantly lower than the rate in non-Hispanic Whites.[3] Comparison with regards to Robin sequence is interesting: in Hispanics,

Table 6. Prevalence of isolated orofacial clefts among Hispanics in California by maternal age groups. (Years 1983-1993).

Maternal age group	Denominator	Prevalence per 1,000 births								
		Cleft lip			Cleft lip and palate			Cleft palate only		
		No.	Rate	95% CI	No.	Rate	95% CI	No.	Rate	95% CI
< 20	148,324	32	0.22	0.15, 0.30	74	0.50	0.39, 0.63	43	0.29	0.21, 0.39
20-24	295,711	77	0.26	0.21, 0.33	184	0.62	0.54, 0.72	67	0.23	0.18, 0.29
25-29	257,714	56	0.22	0.16, 0.28	113	0.44	0.36, 0.53	57	0.22	0.17, 0.29
30-34	148,824	26	0.17	0.11, 0.26	76	0.51	0.40, 0.64	30	0.20	0.14, 0.29
35+	72,544	12	0,17	0.09, 0.29	38	0.52	0.37, 0.72	18	0.25	0.15, 0.39

Table 7. Prevalence of nonsyndromic, nonchromosomal multiple orofacial clefts among Hispanics in California by maternal age groups. (Years 1983-1993).

Maternal age group	Denominator	Prevalence per 1,000 births								
		Cleft lip			Cleft lip and palate			Cleft palate only		
		No.	Rate	95% CI	No.	Rate	95% CI	No.	Rate	95% CI
< 20	148,324	6	0.04	0.01, 0.09	21	0.14	0.09, 0.22	28	0.19	0.13, 0.27
20-24	295,711	10	0.03	0.02, 0.06	53	0.18	0.13, 0.23	42	0.14	0.10, 0.19
25-29	257,714	9	0.03	0.02, 0.07	30	0.12	0.08, 0.17	33	0.13	0.09, 0.18
30-34	148,824	2	0.01	0.00, 0.5	21	0.14	0.09, 0.22	25	0.17	0.11, 0.25
35+	72,544	2	0.03	0.00. 0.10	16	0.22	0.13, 0.36	12	0.17	0.09, 0.29

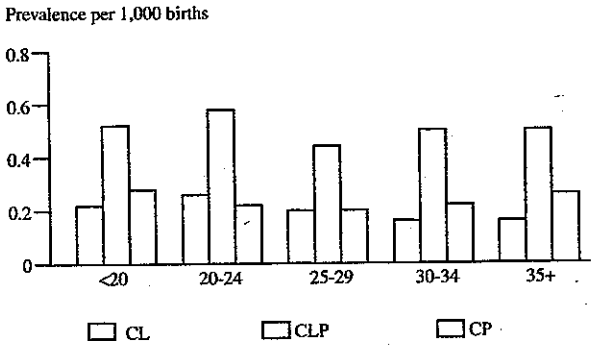

Figure 15. Prevalence of isolated orofacial clefts among Hispanics in California by maternal age groups.

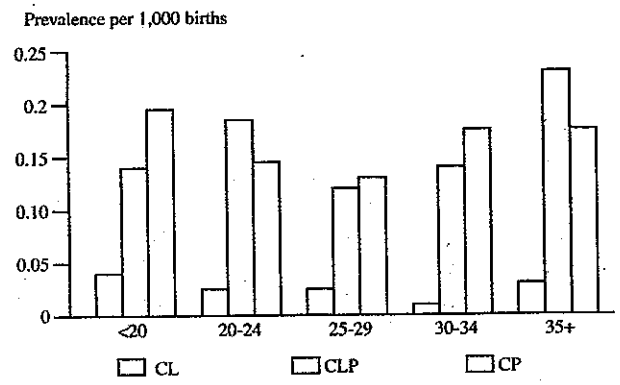

Figure 16. Prevalence of nonsyndromic, nonchromosomal multiple orofacial clefts among Hispanics in California by maternal age groups.

Robin sequence occurs two times less often (0.04/1,000) compared to non-Hispanic Whites, who have the highest prevalence of this condition (0.08/1,000).

Our study shows that in the subgroup of isolated CL±P, CLP occurs in a very high proportion of cases in the Hispanic population. While in non-Hispanic Whites approximately 60% were CLP and the CL:CLP ratio was 0.7193 in Hispanics 70.5% were CLP cases and only 29.5% were CL cases (CL:CLP ratio 0.419). Also rates for CL in Hispanics are significantly lower than in Whites.

Differences in both genetic and environmental factors that very probably exist between populations of the same race, and even between populations of the same ethnic group may explain the differences in the prevalence of clefts as well as differences in CL/CLP ratios.

However, large sample sizes are required to determine if any differences exist. Amidei et al.[19] did not observe any difference in the occurrence of CL±P between non-Hispanic Whites and Hispanics on a sample of 307 children with orofacial clefts out of 381,175 live births. Our sample is larger and did show differences when California Hispanics Whites were compared with California non-Hispanic Whites. However, no significant differences were found when the prevalence of isolated orofacial clefts was calculated for the subgroup of children of Hispanic mothers who were born in Mexico and then moved to California (Table 3).

The prevalence of nonsyndromic, nonchromosomal multiple anomalies with CL±P (CL±P/MCA) was found to be 0.18 per 1,000 births (Table 4). This is the highest rate among Asians, Blacks, and non-Hispanic Whites, [Tolarova and Cervenka, 1998: Asians=0.17/1,000; Blacks=0.16/1,000 non-Hispanic Whites=0.14/1,000). However, for CP/MCA, the prevalence 0.15/1,000 (Table 4.) was the same as for non-Hispanic Whites.[3] (For detailed evaluation of prevalence of orofacial clefts among Asians in California, see Croen et al.[20]).

It has been well established that the sex ratio (male:female ratio) for orofacial clefts is not equal. In Whites, it is significantly increased, favoring males with CL and CLP. More females are affected with CP. We found a predominance of males in CL and CLP cases in both subgroups -isolated and multiples. In CP only in isolated cases, the usual predominance of females was found. Among multiple congenital anomalies with CP a predominance of males was found. Compared to other ethnic groups from California[21] the predominance of males in CL±P was the highest for isolated defects as well as for multiple defects. For isolated CP the sex ratio was the same and for CP/MCA slightly lower compared to non-Hispanic Whites in California.[21]

Parental age has been reported to be associated with several congenital anomalies including cleft lip and palate. The highest risk for having a baby with isolated CL±P was found for mothers 20-24 years old. The risk of having a baby affected with CL±P/MCA (Table 7.) was highest in the subgroup of mothers 35 years old and older. However, for non-Hispanic Whites in California the highest risk for having a baby either with isolated or with multiple CL±P was found for teen-age mothers.[22] We found the highest risk for having a baby affected with either isolated or multiple CP in Hispanic mothers younger than 20 years. The teen-age non-Hispanic White mothers had also the highest risk for having a child with CP/MCA, but not isolated CP where the group at the highest risk were mothers in the age group 25-29 years.[22]

This study presents essential information regarding the epidemiology of orofacial clefts in the Hispanic population in California and can provide a framework for other genetic studies, for genetic counseling, and for studies to determine the causes of the defect and approaches to the prevention of these serious anomalies.

El objetivo de este estudio fue determinar las características epidemiológicas de las hendiduras orofaciales [labio hendido (LH), paladar hendido (PH), labio y paladar hendido (LPH), y hendiduras "atípicas"] y las condiciones en que se presentan entre hispanos. Se analizó una muestra de población básica de 4,433 casos obtenidos de 2,509,881 nacimientos ocurridos en California. De estos, 1,595 (35.98%) correspondieron a 923,578 nacimientos de hispanos en California durante un lapso de 11 años comprendido entre 1983 y 1993. Se clasificaron todos los casos de acuerdo a características previamente presentadas: anormalidades de hendidura aislada, secuencias del defecto primario, aberraciones cromosómicas, síndromes monogénicos, resultados de asociaciones teratógenas conocidas, anomalias congénitas múltiples (ACM) de causa desconocida, o gemelos unidos. La prevalencia de LH±P fue 0.74 por 1,000 nacimientos (LH 0.22/1,000, LPH 0.53/1,000), de PH aislado de 0.23 por 1,000 nacimientos, y de la secuencia de Robin de 0.04 por 1,000 nacimientos. No se encontraron diferencias significativas cuando se calcularon las prevalencias de hendiduras orofaciales aisladas para el subgrupo de niños de madres hispanas que nacieron en México y se mudaron a California. Las anomalías aisladas fueron 57.05% de todas las hendiduras. En la muestra total, se encontraron 3.89% de secuencias, 9.54% de aberraciones cromosómicas, 6.08% de síndromes monogénicos, 1.25% de asociaciones, 22.13% of ACM de etiología desconocida y 0.06% en gemelos unidos. El predominio habitual de varones se encontró en casos de LH y LPH en ambos subgrupos, aislados y múltiples [índice varón:mujer=1.64 (LH, LH/ACM); 1.79 (LPH); 1.71(LPH/ACM)]. En PH sólo, se encontro el predominio habitual de mujeres, (índice varón:mujer=0.76). Entre PH/ACM, se encontró predominio en varones (índice varón:mujer=0.92). La valoración de la muestra por grupos de edades maternos, mostró que el mayor riesgo de tener un niño afectado con LH±P es de 20 a 24 años; el de tener un niño afectado con PH aislado se observó en madres de menos de 20 años; y el de tenerlo con H/ACM fue mayor para LPH en el subgrupo de madres de 35 años o mayores y con PH/ACM en menores de 20 años. Este estudio expone información fundamental relacionada con la epidemiología de hendiduras orofaciales en la población hispana de California, y proporciona un marco para consejo genético, así como para realizar otros estudios enfocados a determinar las causas y la prevención de estas graves anormalidades.

Acknowledgement

Author would like to thank Sally Petersone-Falzone, PhD for her comments and editing of this paper and CBDMP for the data from its registry.

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