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Brief communication (Original)

Epidemiology of cleft lip with or without cleft palate in Thais

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Background: Oral clefts, including cleft lip (CL), CL with cleft palate (CL/CP), and cleft palate only (CPO), are among the most common birth defects, and if left untreated can cause significant morbidity. Causes are complex and involve both genetic and environmental factors. Several studies have demonstrated the highest prevalence of oral clefts being in Asian, white, and African populations. However, there have been very few epidemiological studies of oral clefts in Thais.
Objectives: To describe the epidemiology and factors associated with oral clefts in Thais.
Methods: This retrospective case–control observational study included individuals from numerous regions in Thailand. We reviewed data regarding 784 patients with an oral cleft collected in questionnaires as part of the Thai nationwide Smart Smile and Speech Project from 2006 to 2014. Data regarding patients with oral clefts were analyzed, and compared with data regarding 187 unaffected controls.
Results: Of 784 cases, CL/CP accounted for 59.8%, CPO 21.9%, and CL 18.3%. A family history of oral clefts was detected in all 3 types ($P < 0.001$). Maternal use of any drugs or herbal medicine not prescribed by physicians during pregnancy in cases of CPO ($P = 0.049$) and maternal consumption of alcohol during pregnancy in cases of CL/CP ($P = 0.047$) were significantly higher than that by mothers of controls.
Conclusions*:* CL/CP is the most common type of oral cleft. A family history of oral clefts, and maternal consumption of alcohol or nonprescribed drugs are positively associated with oral clefts in Thais.

Keywords: Cleft lip, cleft palate, oral cleft, Thai

Oral clefts including cleft lip (CL), CL with a cleft palate (CL/CP), and cleft palate alone (CPO) are among the most common congenital malformations of the oral cavity. The prevalence of oral clefts is about 1–2 per 1,000 live births worldwide [1]. The highest prevalence has been reported in Asians, followed by white people of western European ancestry, and Africans [1, 2]. The prevalence of oral clefts in Thais is around 1.1–2.4 per 1,000 live births [3, 4]. If left untreated, individuals with oral clefts experience significant morbidity such as malnutrition because of feeding problems [5-7]. In addition, multiple specialists are required for the appropriate management of patients with oral clefts from infancy to adolescence. Financial and psychosocial issues are also major concerns in families with members affected by oral clefts [8-10]. Several studies have attempted to determine risk factors including genetic, maternal, and other environmental factors contributing to the occurrence of oral clefts [5, 11-14]. These studies were conducted in the hope that strategies could be implemented to reduce the incidence of oral clefts. There have been a few studies reporting the risk factors for oral clefts in Thais. These were conducted in selected regions of the northeastern and southern parts of Thailand [5, 15, 16]. We conducted a retrospective case–control observational study to describe the nationwide epidemiological characteristics and determine other factors that may have contributed to the occurrence of oral clefts. Based on the timing of embryogenesis and

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epidemiology, CPO has been considered a separate entity from CL and CL/CP; we therefore classified oral clefts into CL, CL/CP, and CPO [17, 18].

Materials and methods

Study design

After approval by the institutional review board of the Faculty of Medicine, Chulalongkorn University (certificates of approval Nos. 471/2008 and 493/2013, and institutional review board approval Nos. 216/51 and 227/56), we reviewed data regarding 784 patients with an oral cleft and their mothers as collected in questionnaires as a part of the Smart Smile and Speech Project during 2006–2014 as approved by the Thai Ministry of Public Health, and regarding a group of control patients consisting of 187 unrelated children without oral clefts who had attended King Chulalongkorn Memorial Hospital. The questionnaires had been completed by physicians or trained project assistants after obtaining written informed signed consent from the participants (including patients, controls, and their mothers) as appropriate, consent from a parent or legal guardian where the participant was less the age of consent, and assent from participants where appropriate (usually older than 7 years), in accordance with the Declaration of Helsinki and its contemporary revisions.

Participants

All patients with oral clefts had been examined by pediatricians and pediatric surgeons, and were divided into three groups (CL, CL/CP, and CPO). The patients were from 40 provinces across Thailand and control patients without oral clefts had attended King Chulalongkorn Memorial Hospital (**Table 1**).

Data analysis

We retrospectively reviewed data regarding demographics, maternal use of any drugs or herbal medicine not prescribed by physicians, tobacco and alcohol consumption more than once a week during pregnancy, and family medical history. Categorical data between the case and control groups were compared using a chi-square test. All data were analyzed using IBM SPSS Statistics for Windows, version 22 (IBM Corp, Armonk, NY, USA). $P < 0.05$ was considered significant.

Results

Of 784 patients with an oral cleft, CL/CP was the most common type (59.8%) followed by CPO 21.9% and CL 18.3%. The proportion of affected female patients with CPO was 53.5% and CL 53.2%. By contrast, a higher proportion of male patients with CL/CP were noted (58.3%). Compared with the control group, there was a significant difference in family history of oral clefts in CL, CPO, and CL/CP ($P < 0.001$) and in maternal use of nonprescribed medications during pregnancy in CPO ($P = 0.049$), and maternal consumption of alcohol during pregnancy in CL/CP ($P = 0.047$) (**Table 2**).

Table 1. Number of patients with oral clefts from various regions of Thailand

Region of Thailand	CL	CPO	CL/CP
Northern	39	45	128
Northeastern	29	40	142
Western	–	–	1
Central	20	41	72
Southern	48	38	116
Unidentified	7	8	10
Total (n = 784)	**143**	**172**	**469**

CL, cleft lip; CPO, cleft palate only; CL/CP, CL and cleft palate

Table 2. Characteristics of patients with oral clefts and unaffected controls

Variable	Total	CL (n = 143)	CPO (n = 172)	CL/CP (n = 469)	Control (n = 187)
1. Sex					
Male	500	67 (46.9%)	75 (46.6%)	262 (58.3%)	96
Female	441	76 (53.2%)	86 (53.5%)	188 (41.8%)	91
P^a		$P = 0.42$	$P = 0.38$	$P = 0.11$	
2. Nonprescribed drug use during pregnancy					
No use	847	124 (87.9%)	148 (86.1%)	403 (87.6%)	172
Use	112	17 (12.1%)	24 (14.0%)	57 (12.4%)	14
P^a		$P = 0.17$	$P = 0.049$*	$P = 0.07$	
3. Smoking during pregnancy					
No smoking	942	139 (99.3%)	169 (98.8%)	451 (98.3%)	183
Smoking	13	1 (0.7%)	2 (1.2%)	8 (1.7%)	2
P^a		$P = 0.73$	$P = 0.94$	$P = 0.54$	
4. Alcohol consumption during pregnancy					
None	924	134 (97.8%)	167 (98.2%)	439 (95.9%)	184
More than once per week	27	3 (2.2%)	3 (1.8%)	19 (4.2%)	2
P^a		$P = 0.42$	$P = 0.58$	$P = 0.047$*	
5. Family history of oral clefts					
Positive	158	26 (19.3%)	30 (18.8%)	98 (22.3%)	4
Negative	758	109 (80.7%)	130 (81.2%)	342 (77.7%)	177
P^a		$P < 0.001$	$P < 0.001$	$P < 0.001$	

*$P < 0.05$, [a]chi-square test.

Discussion

We describe some epidemiological characteristics of patients with oral clefts in a large sample size from all parts of Thailand. The most common type of oral clefts was CL/CP 469/784 (59.8%). This finding is consistent with previous studies in Japanese and Chinese populations. However, the proportions differed from those in populations with African ancestry [9, 19, 20]. Several studies found that CLO was the most common type of cleft in populations with African ancestry [10, 19, 21]. We found that oral clefts were more frequent in male patients (male/female; 500/441) as consistent with previous reports [22, 23].

The present study revealed a significantly greater use of nonprescribed drugs by mothers during pregnancy associated with patients with CPO ($P = 0.049$) and maternal alcohol consumption during pregnancy associated with CL/CP ($P = 0.047$). Maternal use of medications during pregnancy was associated with an increased risk of having children with oral clefts in a population from Kosovo [24], while an association between maternal consumption of alcohol and oral clefts was found in populations from Spain [13] and Brazil [11, 12].

We found that a proportion of patients with oral clefts had other family members affected (19.2% in CL, 18.8% in CPO, and 22.3% in CL/CP). A previous study of a population from the southern region of Thailand [25] showed that 17.7% of patients with oral cleft had a family history of oral clefts.

In conclusion, CL/CP is the most common type of oral cleft in the Thai population. Consistent with other populations studied by others, some significant epidemiological and genetic factors, including maternal use of nonprescribed medications and consumption of alcohol during pregnancy, and family history of oral clefts tended to be associated with a higher prevalence of oral clefts.

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Conflict of interest statement

The authors declare that there is no conflict of interest in this research.

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