Characteristics of Orofacial Clefting in Hawai'i

Lily Hoffman-Andrews MS; Jessica M. Tarnowski MS; Sansan Lee MS;
Lianne Hasegawa-Evans MS; Helen L. Lau RN, MS, APRN-Rx;
Joan C. Meister MD; Diane Lynne Ching MD; and Robert Wallerstein MD

Abstract

Orofacial clefts are birth defects that require a multi-disciplinary approach for repair and ongoing management as there are often concomitant chronic health issues. Orofacial clefts can occur as an isolated finding, in combination with other anomalies, or as part of a genetic syndrome. When occurring as part of a genetic syndrome, the complexity of management increases and has lifelong implications for these individuals, their families, and their health care providers. Understanding factors related to the occurrence of syndromic orofacial clefting is important for birth defect research and for health care needs assessment and planning. Many research groups have addressed these issues by studying different populations and focusing on different questions. This study was a retrospective chart review of children with orofacial clefts cared for at a pediatric tertiary care center in Hawai'i to evaluate the proportion of isolated and syndromic clefts in the unique population of Hawai'i. The prevalence of syndromic and isolated clefts were then correlated with ethnicity and compared to the prevalence in other studies. Our goal was to increase knowledge about orofacial clefting in the population of Hawai'i. The proportion of isolated orofacial clefting in a population of patients with orofacial clefting cared for at a craniofacial clinic is similar to birth defect registry data for the Hawaiian Islands (59% vs 58%). Pacific Islanders in our study and prior study have a lower proportion of isolated clefts, suggesting that there are more craniofacial patients with syndromic and complex needs in this population. Further study is needed to clarify the etiologic factors.

Keywords

Hawai'i, Ethnicity, orofacial clefts, syndromic clefts, non-syndromic clefts

Introduction

Orofacial clefts are common congenital malformations of the lip, palate, or both. They may involve the lip, the roof of the mouth (hard palate), the soft tissue in the back of the mouth (soft palate), and the oral cavity which can extend onto the facial structures resulting in oral, facial, and craniofacial deformity. Orofacial clefts generally require surgical repair, and often multiple surgeries are needed to reconstruct the lip and palate. In addition to surgical treatment, individuals need other services including: pediatric care, hearing assessment, speech and language therapy, dental evaluation, orthodontic treatment, genetic services, and psychology or other mental health therapy.[1] The role of the craniofacial team in the management of cleft lip with or without palate is essential. A craniofacial team is a multidisciplinary group which provides consultations, diagnosis, treatment planning, and procedures for a range of craniofacial anomalies and syndromes.[2] Teamwork is highly recommended in the management of persons with orofacial clefts. This team is dedicated to ensuring that persons with the condition are offered the necessary help, care, and support to allow them to have a better life.[3] An accurate diagnosis is critical to the process of counseling families. A cleft lip or palate may negatively impact on an individual's self-esteem, social skills, and behavior.[4]

It has long been known that ethnicity is a factor influencing the occurrence of orofacial clefting with studies documenting varying incidence rates by ethnicity.[1] In 1998, Tolarova and Cervenka reported the occurrence of isolated cleft lip and palate rates among various ethnicities as follows : Caucasians 0.81/1000 livebirths, Asians 0.76/1000 livebirths, Hispanics 0.74/1000 and Blacks 0.41/1000 in a population-based sample of 4,433 cases ascertained from 2,509,881 California births.[5] The nature of the observed ethnic differences in orofacial clefting is not clear, although some researchers suggest a genetic basis. In a 1974 study from Hawai'i, Ching and Chung found that those with Japanese ancestry continued to have an increased birth prevalence of cleft lip with or without cleft palate, while those who are Japanese-Caucasian have a birth prevalence that is intermediate between the Japanese and Caucasian populations, suggesting that the ethnic differences were independent of the environment and that genetics play a significant role in clefting.[3]

Recent studies have evaluated genetic susceptibility loci with single-nucleotide polymorphisms (SNPs) identified by genome-wide studies in individuals of European and Asian ancestry. Results indicate that risk factors differ between populations and confirm the importance of testing putative susceptibility variants in different genetic backgrounds.[4] Known factors include 2p24 near FAM49A, a gene of unknown function, 19q13 near RHPN2, a gene involved in organizing the actin cytoskeleton, 1p36 (PAX7), 1p22 (ARHGAP29), 1q32 (IRF6), 8q24 and 17p13 (NTN1), and 17q23.[5] None of these loci have been identified as exclusive causative agents.[6,7]

Other studies have indicated that the environment may play a key role in the development of clefting. In two separate studies, researchers found that the prevalence of cleft lip with or without cleft palate in Filipino infants born in the Philippines is higher than the prevalence of Filipino infants born in the United States (of note, Filipino families in both studies reported full Filipino ancestry).[8,9] The researchers suggested that environmental factors, in particular the improved socioeconomic status among Filipinos in the United States, may account for a portion of the observed decrease in prevalence.

Hawaii's population represents an ethnically and geographically distinct, diverse population with origins predominantly throughout the Pacific basin.[10] Genetic studies related to orofacial clefts among Pacific Islanders are lacking. The goal of this descriptive study was to determine whether the proportion of isolated facial clefts in the orofacial cleft patient population of the Hawaiian islands is similar to populations in other parts of the world such as Europe, South America, and Asia.

Method/Description

We undertook a retrospective record review of patients who had a clinical genetic evaluation between September 2010 and June 2017 at the Kapi'olani Medical Center for Women and Children (KMCWC) Cleft and Craniofacial Center, a tertiary care center serving the Pacific Islands. Clinical genetics evaluation consisted of a history and record review by a genetic counselor, physical examination by a medical geneticist, and subsequent laboratory testing as indicated by this evaluation. Such laboratory tests included: chromosomal microarray and specific single gene tests if indicated by clinical suspicion of a genetic disorder.

To be included in the chart review, patients must meet all of the following criteria: 1) clinical genetics evaluation completed during the study period, 2) presence of an orofacial cleft lip, cleft palate or both (patients with other conditions as microtia or craniosynostosis were excluded), and 3) availability of self-reported ethnicity information (individuals who were not aware of their ethnic background due to adoption, foster care placement, or death of a parent were excluded).

The patients were stratified into categories of 1) Isolated orofacial clefting that included both isolated cleft lip, isolated cleft palate, and isolated cleft lip and palate, and 2) Orofacial clefting with other anomalies, for these patients a syndromic diagnosis was not known, and 3) Syndromic diagnosis where a specific syndromic diagnosis was known. The diagnoses identified are summarized in Table 1.

Ethnicity was stratified as follows: 1) Pacific Islander Only (included individuals of any combination of just the following ethnicities: Native Hawaiian, Samoan, Tongan, Micronesian); 2) Asian Only (included individuals of any of the combination of the following ethnicities: Japanese, Chinese, Korean, Vietnamese, Filipino); 3) Caucasian Only (including individuals of European ancestry); 4)Mixed Pacific Islander (Mixed ethnicity with Pacific Islander ancestry); and 5) Mixed ethnicity without Pacific Islander. Groups 1, 2, and 3 fully reported those respective ethnicities and none from other categories.

The proportion of patients with isolated orofacial clefts, those with orofacial clefts with other anomalies, and those with syndromic diagnoses was calculated for each of the above ethnicity categories. Tests of statistical significance with ANOVA and *P*-values were then completed using Good Calculators Mathematics Statistics and Analysis Calculators software (https://goodcalculators.com/statistics-calculators/).

Table 1. Types of Syndromes Noted and Number of Patients
Chromosome microduplication/microdeletion = 3
Branchio-Oculo-Facial syndrome = 1
CHARGE syndrome = 2
Cri du chat = 1
Diabetic embryopathy = 4
Diamond Blackfan anemia = 1
Down syndrome = 1
Goldenhar syndrome = 3
Kabuki syndrome = 1
Sotos syndrome = 1
Spondylocostal dysostosis = 1
Stickler syndrome= 5
Treacher Collins = 1
Van der Woude = 2
22q11.2 deletion syndrome = 3
Waardenburg = 1
Wolf-Hirschhorn syndrome = 1

Results

The total population included 308 patients and was separated into ethnic categories by self-report of Pacific Islander Only 10.4% (n=32), Asian Only 27.3% (n=84), Caucasian Only 7.8% (n=24), Mixed ethnicity with Pacific Islander ancestry 42.2%(n=130), and Mixed ethnicity without Pacific Islander ancestry 12.3% (n=38). Pacific Islander Only patients had 59.3% (n=19) isolated orofacial clefting; clefting with other anomalies accounted for 25.0% (n=8) and syndromic diagnosis accounted for 15.6% (n=5). Asians Only had 71.4% (n=60) isolated orofacial clefting; clefting with other anomalies accounted for 17.9% (n=15) and syndromic diagnoses accounted for 10.7% (n=9). Caucasian Only had 75% (n=18) isolated clefting; orofacial clefting with other anomalies accounted for 16.7% (n=4). Mixed ethnicity with Pacific Islander had 70.8% isolated clefting; orofacial clefting with other anomalies accounted for 16.9% (n=22); syndromic diagnoses accounted for 12.3% (n=16). Mixed ethnicity without Pacific Islander had 76.3% isolated clefting; orofacial clefting with other anomalies accounted for 10.5% (n=4) (Table 2). When stratified by ethnicity, the proportion of isolated orofacial clefts varied from 59.3% to 76.3%, with Pacific Islanders Only being the lowest and Mixed Ethnicity without Pacific Islander being the highest (Table 3).

The proportion of isolated orofacial clefts did not differ significantly between the five categories of ethnic groups (F-statistic value of 0.9895 and *P*-value = .46). In addition, the total per-

Table 2. Tabulation of Clinical Findings by Ethnicity					
Total N = 308	**Pacific Islander only n (%)**	**Asian Only n (%)**	**Caucasian Only n (%)**	**Mixed Pacific Islander n (%)**	**Mixed Without Pacific Islander n (%)**
Isolated Orofacial clefting including isolated cleft lip and isolated cleft palate	19 (59.3%)	60 (71.4%)	18 (75.0%)	92 (70.8%)	29 (76.3%)
Orofacial clefting plus additional anomalies	8 (25.0%)	15 (17.9%)	4 (16.7%)	22 (16.9%)	4 (10.5%)
Syndromic diagnoses	5 (15.6%)	9 (27.3%)	2 (8.3%)	16 (12.3%)	5 (13.2%)
Total	32 (10.4%)	84 (27.3%)	24 (7.8%)	130 (42.2%)	38 (12.3%)

Cleft with additional anomaly = cleft with a major anomaly (requiring ongoing developmental or medical intervention or evaluation), but no confirmed syndromic diagnosis
Pacific Islander Only = Hawaiian, Samoan, Micronesian
Asian Only = Japanese, Chinese, Korean, Vietnamese Filipino
Caucasian Only = Caucasian only
Mixed Pacific Islander = Pacific Islander plus any other ethnicity
Mixed Without Pacific Islander = More than one ethnicity without Pacific Islander

Table 3. Proportion of Non-syndrome Orofacial Clefts Among Those with Orofacial Clefts in Hawaiian Populations and Published Studies		
Current Study		
	Pacific Islanders	59%
	Asians	71%
	Caucasians	75%
	Mixed Pacific Islanders and Other	70%
	Mixed Ethnicity without Pacific Islanders	76%
Published Studies	**Population Studied**	
Forrester and Merz[17]	Hawaiian Islands*	58%
IPTOC[18]	International	77%
Mossey, et al[19]	International	88%
Croen, et al[7]	California	74%
Milerad, et al[16]	Sweden	72%
Eurocat[20]	Mixed European	66%
Rittler, et al[21]	Latin America	76%

*Mixed ethnicity population from birth certificate data

centage of individuals with isolated orofacial clefts involved in our study (71%) fell within the range of percentages of isolated orofacial clefting reported in other studies (58-88%) (Table 3).

Discussion

Many epidemiologic studies have been conducted on the prevalence of isolated orofacial clefts and the variation among different ethnic groups.[1,2,3,7,8,9,13,14,15,19,20] Clefting has been shown to be consistently more common in the Native American population and becomes progressively less common in Asians, Caucasians, and Africans.[5,7,11] Although our data did not show a statically significant difference between the prevalence of isolated orofacial clefting among the different ethnic groups included, our prevalence estimates are consistent with past studies. We found the highest rates of isolated orofacial clefting among Asians and Pacific Islanders and the lowest rate in Caucasians.

The percentage of Asians and Pacific Islanders with isolated orofacial clefting observed in our data could simply be a reflection of the ethnic variation observed within Hawaii's population. According to the 2017 US Census Bureau, the population of Hawai'i is made up of 37.8% of individuals who self-report as Asian only, 25.7% of individuals who self-report as Caucasian only, 10.2% of individuals who self-report as Pacific Islander only, and 23.8% who self-report as being of two or more races.[12] Thus, Asian and Pacific Islanders represent some of the largest ethnic groups in Hawai'i. There may be limits on the comparability of ethnicity data in a census to that reported in a medical setting.

The total percentage of isolated orofacial clefting in our study (71%) was similar to the percentage of isolated clefting reported in other studies (Table 3). Likewise, the percentage of orofacial clefts associated with a syndrome or additional anomaly observed in our study (29%) was very consistent with those reported by other studies.[2,14,15,16] Of note, our reported prevalence of orofacial clefts associated with a syndrome or additional anomaly is much lower than that reported by Forrester and Merz (2004), where 42% had an orofacial cleft as part of a syndrome or as one of multiple anomalies. Their study population was birth defects registry data, which included non-viable individuals with elective terminations and fetal deaths, the majority of which were not isolated, and this likely increased the number of syndromic clefts. Our study population included only viable individuals, which may select more isolated clefts.

Our data is consistent with Forrester and Merz's (2007) study indicating a higher incidence of syndromic clefting in Pacific Islanders.[17] Because Pacific Islanders, historically, come from genetically isolated populations, this could reflect a unique genetic profile that confers increased risk for syndromic orofacial clefting. More research is required to further understand this trend.

Conclusion

Within our population, we observed that syndromic clefting is more common among the Pacific Islanders than among the orofacial cleft population in other ethnic groups (15.6% vs 8.3-13.2%). Our study was comparable to the prior study from birth defects registry data (Forrester and Merz[17]) where 58% of orofacial cleft cases were categorized as isolated; the present study identifies 59% as presenting as isolated. In other international studies the proportion of isolated clefting ranges from 66-88% (See Table 3). Therefore, the proportion of more medically complex individuals within the orofacial cleft population is higher in the current study. This would have implications for medical resource management for individuals with orofacial clefting in Hawai‘i as more medically complex individuals would require greater utilization of services. As the scientific knowledge of susceptibility factors increases, future studies may be able to further clarify the etiologic factors related to this trend.

Conflict of Interest

None of the authors identify any conflict of interest.

Authors' Affiliations:
- Hawai'i Community Genetics, Honolulu, HI (LH-A, JMT, SL,LH-E, RW)
- Cleft and Craniofacial Center, Department of Pediatrics, Kapi'olani Medical Center for Women and Children, Honolulu, HI (SL, LH-E, HLL, JCM, DLC,RW)

Correspondence to:
Robert Wallerstein MD; Email: robert.wallerstein@kapiolani.org

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