# Ophthalmologic Abnormalities in Cleft Lip and Palate

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## Purpose

The failure of fusion of facial processes that causes cleft lip and palate (CLP) may also result in ocular abnormalities, given their proximity and simultaneous embryonic development. The purpose of this study was to examine ophthalmologic findings of patients with CLP.

**Table 1.** Demographic data, clefts characteristics, and associated syndromes of 687 patients with cleft lip and/or palate (CLP).[a]

| Variable | N (%) |
|---|---|
| Age at ophthalmologic examination (years) | 4.4 ± 4.5 |
| *Gender* | |
| Female | 345 (50.2) |
| Male | 342 (49.8) |
| *Cleft characteristics* | |
| Isolated cleft lip | 41 (6) |
| Isolated cleft palate | 465 (67.7) |
| Combined cleft lip and palate | 181 (26.3) |
| *Cleft palate classification* | |
| Any cleft palate | 646 (94) |
| Submucosal | 128 (19.8) |
| Veau I | 99 (15.3) |
| Veau II | 243 (37.6) |
| Veau III | 103 (15.9) |
| Veau IV | 72 (11.1) |
| *Associated syndrome or genetic variant* | |
| None | 290 (42.2) |
| Pierre Robin sequence | 86 (12.5) |
| 22q11.2 deletion syndrome | 75 (10.9) |
| Goldenhar syndrome | 11 (1.6) |
| Van der Woude syndrome | 10 (1.5) |
| TP63-related disorder | 7 (1.0) |
| Treacher Collins syndrome | 4 (0.6) |
| Hemifacial microsomia | 3 (0.4) |
| Trisomy 13 | 2 (0.3) |
| Trisomy 18 | 1 (0.1) |
| Other | 197 (28.7) |

[a]Continuous variables are presented as mean ± standard deviation, and categorical variables are presented as N (%).

## Methods

We performed a retrospective review of patients diagnosed with CLP who underwent ophthalmologic examination from 2009 to 2020 at the Children's Hospital of Philadelphia. Demographic information, ophthalmologic findings, genetic data, and cleft characteristics were collected. Primary outcomes were the type and incidence of ophthalmic disorders and their associations with CLP anatomical and syndromic/genetic risk factors.

## Results

Among 687 included patients, the most common ocular disorders were refractive errors (41.6%), strabismus (30.9%), and nasolacrimal duct obstruction (10.5%). The incidence of nasolacrimal duct obstruction was highest in bilateral cleft lip (22.7%), followed by unilateral cleft lip (10.2%) and no cleft lip (8.6%). Subjects with an associated syndrome were more likely to have strabismus, refractive error, vitreoretinal pathologies, nerve pathology, lagophthalmos, and chorioretinal coloboma. Additionally, patients with Pierre Robin sequence were more likely to have refractive error and vitreoretinal pathologies.

**Table 2.** Ocular and oculofacial abnormalities in 687 patients with cleft lip and/or palate.[a]

| Variable | Total | Nonsyndromic | Syndromic | P-value[b] |
|---|---|---|---|---|
| No. of patients | 687 | 290 | 397 | |
| Vision impairment | 60 (8.7) | 257 (88.6) | 370 (93.2) | **0.04**[c] |
| Refractive error | 286 (41.6) | 106 (36.6) | 180 (45.3) | **0.02** |
| Amblyopia | 173 (25.2) | 66 (22.8) | 107 (27.0) | 0.21 |
| *Strabismus* | | | | **0.02** |
| Esotropia | 84 (12.2) | 28 (9.7) | 56 (14.1) | |
| Exotropia | 128 (18.6) | 45 (15.5) | 83 (20.9) | |
| *Orbital, adnexal, and lacrimal disorders* | | | | |
| Microphthalmia/anophthalmia | 13 (1.9) | 6 (2.1) | 7 (1.8) | 0.77 |
| Proptosis | 2 (0.3) | 1 (0.3) | 1 (0.3) | 0.82 |
| Dermoid cyst | 2 (0.3) | 0 (0.0) | 2 (0.5) | 0.23 |
| Hypertelorism | 11 (1.6) | 2 (0.7) | 9 (2.3) | 0.10 |
| Other orbital diagnoses | 4 (0.6) | 3 (1.0) | 1 (0.3) | 0.18 |
| Lacrimal disorder | 72 (10.5) | 23 (7.9) | 49 (12.3) | 0.06 |
| *Eyelid pathology* | | | | |
| Ptosis | 47 (6.8) | 17 (5.9) | 30 (7.6) | 0.38 |
| Chalazion | 15 (2.2) | 7 (2.4) | 8 (2.0) | 0.72 |
| Lagophthalmos | 18 (2.6) | 3 (1.0) | 15 (3.8) | **0.03** |
| Entropion | 6 (0.9) | 2 (0.7) | 4 (1.0) | 0.66 |
| Ectropion | 5 (0.7) | 2 (0.7) | 3 (0.8) | 0.91 |
| Distichiasis | 5 (0.7) | 1 (0.3) | 4 (1.0) | 0.31 |
| Trichiasis | 3 (0.4) | 1 (0.3) | 2 (0.5) | 0.76 |
| Blepharophimosis | 2 (0.3) | 1 (0.3) | 1 (0.3) | 0.82 |
| Eyelid retraction | 1 (0.1) | 1 (0.3) | 0 (0.0) | 0.24 |
| Other eyelid diagnoses | 16 (2.3) | 9 (3.1) | 7 (1.8) | 0.25 |
| Ocular surface pathology | 72 (10.5) | 26 (9.0) | 46 (11.6) | 0.27 |
| Blepharitis | 8 (1.2) | 3 (1.0) | 5 (1.3) | 0.79 |
| Optic nerve pathology | 66 (9.6) | 24 (8.3) | 42 (10.6) | 0.31 |
| Nerve pathology[d] | 55 (8.0) | 13 (4.5) | 42 (10.6) | **0.004** |
| Chorioretinal or vitreoretinal pathologies[e] | 47 (6.8) | 11 (3.8) | 36 (9.1) | **0.007** |
| Nystagmus | 36 (5.2) | 10 (3.4) | 26 (6.5) | 0.07 |
| *Coloboma* | | | | |
| Optic nerve coloboma | 21 (3.1) | 6 (2.1) | 15 (3.8) | 0.20 |
| Chorioretinal coloboma | 10 (1.5) | 1 (0.3) | 9 (2.3) | **0.04** |
| Iris coloboma | 10 (1.5) | 3 (1.0) | 7 (1.8) | 0.43 |
| Eyelid coloboma | 3 (0.4) | 0 (0.0) | 3 (0.8) | 0.14 |
| Glaucoma | 18 (2.6) | 10 (3.4) | 8 (2.0) | 0.25 |
| Lens pathology | 15 (2.2) | 6 (2.1) | 9 (2.3) | 0.86 |
| Other ophthalmic diagnoses | 90 (13.1) | 21 (7.2) | 69 (17.4) | **0.0001** |

[a]All data presented as N (%).
[b]P-value relates to comparison of syndromic vs. nonsyndromic subjects using chi-squared test.
[c]P-values < 0.05 are bolded.
[d]Includes cranial nerve (excluding optic nerve) palsy, gaze palsy, Horner's syndrome, anisocoria, central visual impairment, delayed visual maturation, color blindness, internuclear ophthalmoplegia, Mobius syndrome, and pseudotumor cerebri syndrome.
[e]Includes retinal detachment, retinal tear, chorioretinal coloboma, vitreous hemorrhage, retinal/preretinal hemorrhage, choroidal hemorrhage, retinopathy of prematurity, maculopathy/macular dystrophy, pigmentary retinopathy/retinal dystrophy, lattice degeneration, persistent hyperplastic primary vitreous, Coat's disease, degenerative myopia with choroidal neovascularization, epiretinal membrane, and vitreous floater/vitreous syneresis.

## Conclusions

This study demonstrates an association between cleft severity and nasolacrimal duct obstruction. While our methodology precludes assignation of causality, this is possibly due to the disruption of fusion of facial processes that occurs in cleft lip and/or palate, which may also impact the development of the orbit and ocular adnexa during embryogenesis. Heightened awareness of ocular pathology may advance multidisciplinary care for patients with CLP.

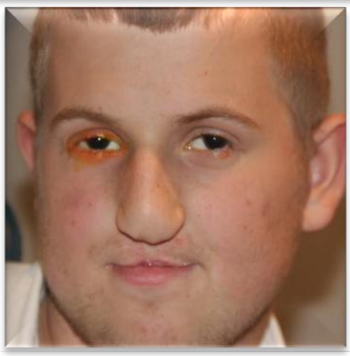

**Figure 1**. A 15-year-old patient with a history of bilateral cleft lip and palate associated with ectrodactyly ectodermal dysplasia-cleft (EEC) syndrome who was diagnosed with right-sided ptosis, esotropia, and congenital right nasolacrimal duct obstruction and treated with dacryocystorhinostomy.

**Figure 2**. A 21-year-old patient with a history of Pierre Robin sequence and cleft palate with diagnoses of high myopia and exotropia.

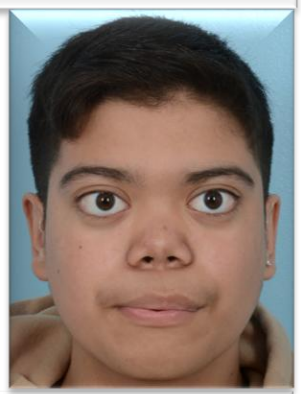

**Figure 3.** 13-year-old patient with a history of bilateral cleft palate associated with Marshall syndrome and diagnoses of proptosis and hypertelorism.