Eye (2002) 16, 710–714

www.nature.com/eye

CLINICAL STUDY

# Characteristic ocular findings in Asian children with Down syndrome

JH Kim[1], J-M Hwang[1,2], HJ Kim[3] and YS Yu[1]


## Abstract

*Aims/Purpose* **To identify the characteristic ocular findings in Asian children with Down syndrome.**

*Methods* **A total of 123 Korean children with Down's syndrome between 6 months and 14 years of age were examined for ocular findings from March 1999 to April 2000. Ocular examinations including visual acuity assessment, slit-lamp biomicroscopy, ocular motility, cycloplegic refraction, and ophthalmoscopy were performed.**

*Results* **The ocular findings in decreasing prevalence were the following: upward slanting of the palpebral fissure (78 patients, 63%), epicanthus (75 patients, 61%), epiblepharon (66 patients, 54%), astigmatism (38 patients, 31%), hyperopia (35 patients, 28%), myopia (31 patients, 25%), strabismus (31 patients, 25%, 18 esotropia and 13 exotropia), nystagmus (27 patients, 22%), nasolacrimal duct obstruction (21 patients, 17%), blepharoconjunctivitis (20 patients, 16%), retinal abnormalities (18 patients, 15%), cataract (four patients, 13%), and glaucoma (one patient, 0.8%). Brushfield spots and keratoconus were not found.**

*Conclusion* **Asian children with Down syndrome demonstrate unreported, high incidence of epiblepharon, the high rate of exotropia, and essentially no notable Brushfield spots, which are in contrast to the ocular findings in Caucasian patients with Down syndrome.**


*Eye* (2002) **16,** 710–714. doi:10.1038/sj.eye.6700208

*Keywords:* Down syndrome; epiblepharon; ocular findings; Asian children

[1]Department of Ophthalmology College of Medicine Seoul National University & Clinical Research Institute Seoul National University Hospital Seoul, Korea

[2]Department of Ophthalmology Seoul Municipal Boramae Hospital Seoul, Korea

[3]Department of Pediatrics Seoul Municipal Boramae Hospital Seoul, Korea

Correspondence: J-M Hwang, MD Department of Ophthalmology Seoul Municipal Boramae Hospital affiliated with Seoul National University Hospital 395, Sindaebang-2-dong Dongjak-ku Seoul 156-707, Korea Tel: 82 2 840 2126 Fax: 82 2 831 2826 E-mail: hjm@snu.ac.kr

Received: 22 October 2001
Accepted: 22 March 2002

## Introduction

Down syndrome (DS) is the most common chromosomal anomaly.[1] Numerous ophthalmic features have been reported, including abnormalities of the eyelid, cornea, iris, lens, retina, and optic disc, as well as ametropia, amblyopia, strabismus, and nystagmus. [2–17] The incidence of each ocular abnormality varies in different studies.[2–17] Most reported studies of ocular findings in DS have been performed in Caucasians. [2–15] There are only a few reports in the literature that make reference to ocular findings in Asian patients with DS. [16,17] In the present study, we prospectively studied the ophthalmic features of Korean children with DS in order to determine the characteristic ocular abnormalities with DS and to detect any differences between them and Caucasian children with DS.

## Patients and methods

The current study consisted of totally noninstitutionalized, home reared Korean children with DS seen in an outpatient setting. Most of the children were from the Parents Association for DS for the ophthalmologic examination. The patients were not recruited for this study. Whether the type of chromosomal abnormality was trisomy 21, translocation, or mosaicism was not known in each case. A specialized examination sheet for the patients with DS was prepared, where all the reported ocular features were printed for check-up.

A total of 123 Korean children (81 boys and 42 girls) with DS between 6 months and 14 years of age were examined by one of the authors (JMH) for ocular findings from March 1999 to April 2000.

The mean and median age of the children was 6.5 and 5 years, respectively. The age distribution was as follows: 6 months to 3 years ($n = 40$), 4–6 years ($n = 43$), 7–9 years ($n = 34$), and more than 9 years ($n = 6$).

The ocular examinations included a visual acuity assessment, slit-lamp biomicroscopy,

ocular motility using the alternate cover uncover test with/without prism, cycloplegic refraction, and ophthalmoscopy. If the children were uncooperative during the evaluation, they were sedated for the refraction, retinoscopy and slit-lamp examination. The palpebral fissure was evaluated by placing a clear plastic straight-edged ruler across the bridge of the nose at the level of both inner canthi, and measuring the vertical displacement of the outer canthi. Upward slanting fissures were defined as 2 mm or more above the horizontal line.

The eyelid margin and conjunctiva were assessed for abnormalities such as blepharitis and conjunctivitis. The presence of keratoconus or iris abnormalities such as Brushfield's spots and stromal hypoplasia was also evaluated. Cataracts were defined as any opacity of the lens. The presence of cilia touching cornea and the amount of resulting corneal erosion were evaluated with a slit lamp biomicroscope before and after fluorescein instillation.

The diagnosis of nasolacrimal duct obstruction was based on a history of epiphora or recurrent mucopurulent discharge since infancy and by the reflux of mucus with the pressure over the lacrimal sac. Cycloplegic refraction was performed in all patients, regardless of age, 45 min after three to five instillations of one drop of cyclopentolate 1%. Emmetropia was defined as a refractive error between −0.75 diopter (D) and +0.75 D spherical equivalent. Myopia was defined as less than −0.75 D spherical equivalent, and hyperopia was defined as more than +0.75 D spherical equivalent. Astigmatism was defined as refractive error more than ±0.75 D of the cylinder.

Indirect and direct ophthalmoscopy after cycloplegic retinoscopy was used to examine the retina, choroid, and optic disc, and included an assessment of the vessels in relation to the optic disc.

## Results

The overall incidence of ocular abnormalities in the Korean children with DS was 91% (112/123). The ocular findings are summarized in Table 1. Upward slanting of the palpebral fissure was the most common ocular finding (78 patients, 63%), followed by epicanthus (75 patients, 61%).

Epiblepharon presumably caused by pushing epicanthal fold was detected in 66 patients (54%), and was most commonly on the medial portion of the upper eyelid (67%), followed by on the upper and lower eyelids (18%), and on lower eyelid only (15%) (Table 2). Multiple punctate corneal erosion was accompanied in 58 patients (88%). Of these, surgical correction was recommended in 18 patients. In most cases, the corneal erosions became more evident with pushing the epicanthal fold to the nose and fluorescein dye staining. The incidence of epiblepharon was as follows: 6 months to 3 years (17 patients, 43%), 4–6 (28 patients, 65%), 7–9 years (17 patients, 50%), and more than 9 years (four patients, 44%).

**Table 1** Ocular abnormalities in 123 patients with Down syndrome

| *Ocular abnormalities* | *Number of patients* | *%* |
|---|---|---|
| Slanting fissures | 78 | 63 |
| Epicanthus | 75 | 61 |
| Epiblepharon | 66 | 54 |
| Astigmatism | 38 | 31 |
| Hyperopia | 35 | 28 |
| Myopia | 31 | 25 |
| Strabismus | 31 | 25 |
| Nystagmus | 27 | 22 |
| Nasolacrimal duct obstruction | 21 | 17 |
| Blepharoconjunctivitis | 20 | 16 |
| No. of retinal vessels ≥ 18[a] | 16 | 13 |
| Lens opacities | 4 | 3 |
| Focal retinal pigment epithelial hyperplasia | 2 | 2 |
| Glaucoma | 1 | 0.8 |
| Corneal opacities | 1 | 0.8 |

[a]Eighteen or more retinal vessels crossing the margin of the optic nerve head and extending at least one disc diameter into the periphery.

**Table 2** Eyelid involvement in 123 patients with Down syndrome

| *Eyelid involved* | *Number of patients* | *%* |
|---|---|---|
| Unilateral or bilateral | | |
| Unilateral | 12 | 18 |
| Bilateral | 54 | 82 |
| Upper or lower | | |
| Upper only | 44 | 67 |
| Upper and lower | 12 | 18 |
| Lower only | 10 | 15 |

The refractive status of the patients is shown in Table 3. Of the 123 patients studied, 38 (31%) had astigmatism, six of whom had equal or greater than 3 D of astigmatism. Hyperopia and myopia were found to be present in 35 (28%) and 31 patients (25%), respectively. Among them, ametropia of more than 3 D was found in 33 patients (27%).

Strabismus was present in 31 patients (25%), 18 of whom had esodeviations and 13 of whom had exodeviations (Table 4). Nystagmus was observed in 27 patients (22%), usually in the horizontal-pendular type. Blepharoconjunctivitis was present in 20 patients (16%). Nasolacrimal duct obstruction was noted in 21 patients (17%). Lens opacities were diagnosed in four patients

**Table 3** Refractive status of 123 patients with Down syndrome

| *Refractive status* | *Number of patients* | *%* |
|---|---|---|
| Emmetropia | | |
| (−0.75 D to +0.75 D) | 57 | 46 |
| Hyperopia | | |
| (+1.00 D to +2.75 D) | 20 | 16 |
| (+3.00 D to +5.75 D) | 10 | 8 |
| (≥+6.00 D) | 5 | 4 |
| Myopia | | |
| (−1.00 D to −2.75 D) | 13 | 11 |
| (−3.00 D to −5.75 D) | 10 | 8 |
| (≤−6.00 D) | 8 | 7 |
| Astigmatism | | |
| (±1.00 D to ±2.75 D) | 32 | 26 |
| (≥±3.00 D) | 6 | 5 |

**Table 4** Incidence of strabismus, and exotropia in the whole strabismus

| | *Incidence of strabismus* | *Eso:Exo:Hyper* | *Incidence of exotropia in whole strabismus* |
|---|---|---|---|
| Present study | 31/123 (25%) | 18:13 | 41.9% |
| Berk *et al*[2] | 12/55 (22%) | 11:1 | 8.3% |
| Caputo *et al*[4] | 107/187 (57%) | 97:4:6 | 0.9% |
| da Cunha & Moreira[6] | 57/152 (38%) | 51:2:4 | 3.5% |
| Hiles *et al*[7] | 42/123 (34%) | 34:8 | 19.0% |
| Eissler & Longenecker [9] | 176/396 (44%) | 176:0 | 0% |
| Shapiro & France[11] | 23/53 (13%) | 22:1 | 4.3% |
| Lowe[12] | 22/67 (33%) | 22:0 | 0% |
| Wong & Ho[17] | 28/140 (20%) | – | – |

Eso, Esotropia; Exo, Exotropia; Hyper, Hypertropia.

(3%). Glaucoma and corneal opacity were each present in one patient.

On fundus examination, 16 patients (13%) exhibited 18 or more vessels crossing the optic nerve head margin and extending at least one disc-diameter towards the retinal periphery. Focal hyperplasia of the retinal pigment epithelium was present in two patients. Keratoconus and iris abnormalities such as Brushfield's spots and stromal hypoplasia were not found in any of the patients.

## Discussion

This study shows the differences of the ocular findings in DS according to race and age. The overall incidence of ocular abnormalities in Korean children with DS (91%) was markedly higher than previously reported (Table 5). [2–17] This might be due to the preparation of a special examination sheet for DS documenting every reported ocular finding, slit-lamp biomicroscopy (before and after fluorescein instillation), cycloplegic refraction, and indirect ophthalmoscopic examination for every patient. The ocular findings in Korean children with DS are characterized as an unreported, high incidence of epiblepharon, the highest rate of exotropia and no cases of Brushfield spots. Although the ocular features of DS have been described in several studies (Table 4),[2–17] we could not find any reference to epiblepharon with DS in a computerized search utilizing Medline. It is surprising that epiblepharon has not been reported in other studies given the frequency in this study. In this study, the incidence of epiblepharon was 54%, which is much higher than that of 9.1%[18] in non-DS Asian children. We speculate that the reason for epiblepharon in DS may be that the presence of epicanthal fold pushes the cilia of the upper lid to the cornea. Every case of epiblepharon in DS was accompanied by the epicanthal fold that pushed the cilia of the upper lid or lower lid or both to the cornea.

The incidence and clinical manifestation of epiblepharon with DS are much different from those in non-DS Asian children. Three major differences were found. First, in non-DS Asian children with epiblepharon, the medial part of the lower eyelid was most commonly involved, and the upper eyelid, the least commonly involved.[18] However, in the epiblepharon with DS, the upper eyelid was characteristically most commonly involved. Second, the incidence of epiblepharon in non-DS Asian children, decreases with age, and only 4.2% showed epiblepharon after 7 years of age.[18] In contrast, the incidence of epiblepharon did not decrease with age much among the patients with DS, and 53% of the patients after 7 years of age still showed epiblepharon. Third, photophobia or epiphora, a common symptom of epiblepharon, was noticed much less commonly in DS children with multiple corneal punctate epithelial erosions than non-DS Asian children in the same situation. Most of the mothers of DS children with epiblepharon had not noticed photophobia or epiphora. A decreased corneal sensitivity or the fact that most of the epithelial erosions were not exposed, covered by the epicanthal fold might contribute to the difference.

The incidence of strabismus in our study was 25%, which is similar to that in other studies from Hong Kong (20%)[17] or Turkey (22%) (Table 4).[2] However, the prevalence of exotropia in the whole strabismus was 42%, in contrast with the data in all other reports, which range from 0% to 19% (Table 4).[2–12,16] Asians are known to have a higher prevalence of exotropia than

**Table 5** Comparison of ocular findings in previous studies with our findings

| | *Present study* | *Wong & Ho (1997)*[17] | *da Cunha & Moreira (1996)*[6] | *Berk et al (1996)*[2] | *Caputo et al (1989)*[4] | *Shapiro & France (1985)*[11] |
|---|---|---|---|---|---|---|
| Number of the patients | 123 | 140 | 152 | 55 | 187 | 53 |
| Nationality | Korea | Hong Kong | Brazil | Turkey | US | US |
| Range of age (years) | 0–14 | 0–13 | 0–18 | 0–25 | 0–26 | 7–36 |
| Mean age (years) | 6.5 | 3.74 | – | 7.2 | 5.8 | 17.4 |
| Upward slanting (%) | 78 (63) | 140 | 125 (82) | – | – | 47 (89) |
| Epicanthus (%) | 75 (61) | 140 | 92 (61) | 13 (24) | – | – |
| Epiblepharon (%) | 66 (54) | – | – | – | – | – |
| Refractive errors (%) | 104 (85) | 137 (98) | 149 (98) | 60 | 122 (65) | 35 |
| Hyperopia | 35 | 42 | 39 | 29 | 39 | 17 |
| Myopia | 31 | 12 | 19 | 7 | 42 | 18 |
| Astigmatism | 38 | 8 | 91 | 24 | 41 | 12 |
| Mixed | | 75 | | | | |
| Strabismus (%) | 31 (25) | 28 (20) | 57 (38) | 12 (22) | 107 (57) | 23 (43) |
| Esotropia | 18 | | 51 | 11 | 97 | 22 |
| Exotropia | 13 | | 0 | 1 | 4 | |
| Hypertropia | 0 | | 4 | 0 | 6 | |
| Nystagmus (%) | 27 (22) | 15 (11) | 28 (18) | 7 (13) | 55 (29) | 5 (9) |
| Nasolacrimal duct obstruction (%) | 21 (17) | – | 46 (30) | 12 (22) | 9 (5) | – |
| Blepharitis/conjunctivitis (%) | 20 (16) | 8 (7) | 45 (30) | 19 (35) | – | 25 (47) |
| Number of retinal vessels ≥18 (%) | 16 (13) | 16 | 42 | 21 (38) | – | – |
| Lens opacities (%) | 4 (3) | 4 | 20 (13) | 11 (20) | 21 (11) | 7 (13) |
| Focal RPE hyperplasia (%) | 2 (2) | – | – | – | | – |
| Glaucoma (%) | 1 (0.8) | 1 | – | – | 10 (5) | – |
| Corneal opacities (%) | 1 (0.8) | – | – | – | – | – |
| Keratoconus (%) | 0 (0) | 0 (0) | – | – | – | 8 (15) |
| Brushfield spots | 0 (0) | 0 (0) | 79 (52) | 20 (36) | – | 43 (81) |

Caucasians or Africans in a normal population.[19] Racial factors may play a role in this strikingly high incidence.

Upward slanting of the palpebral fissures, the most frequent ocular findings, was present in 78 patients (63%). Epicanthal folds, the second most prevalent feature, were found in 75 patients (61%). The prevalence of these two abnormalities has been reported as low as 9%[3] and as high as 100% (Table 5).[16] This large variation may be related to age and racial factors. Several authors have reported a decreasing prevalence with increasing age.[3,9,12]

The incidence of nasolacrimal duct obstruction ranges from 5 to 30% according to the age distribution of each study (Table 5).[2,4–6] In our study, it was found in 21 patients (17%), representing the low median age of our patients.

Nystagmus was present in 27 patients (22%), which is in accordance with previous reports of 4–30% (Table 5).[2,4,6–8] The patients with nystagmus in the present study usually had the refractive errors, which is in line with other studies reporting that the nystagmus was associated with refractive errors.[9,17]

The incidence of lens opacities (4%) was similar to that in the studies of Roizen *et al* (5%)[10] and Wong and Ho (4%),[17] but quite lower than the 11–86% of other reports (Table 5).[2,4–6,9–16] This varying incidence rate might be related to the differences in age distribution and diagnostic criteria. Cataracts in DS usually appear between 12 and 15 years of age and almost never before 6 years of age.[9,13] In our study, 84% of the children were under 8 years of age, and only two were over 12 years of age.

The incidence of keratoconus in DS varies between 0 and 30%.[2,4–6,9–12] It was not surprising that there was no keratoconus in our group because the median age was very low. Our patients might still be too young for keratoconus to develop. As the children mature, the serial monitoring of this feature might be helpful in detecting any genuine differences between our group and those in the other studies.

Brushfield spots, lighter colored iris, and peripheral stromal hypoplasia are known to be common, but are not necessarily diagnostic signs in DS.[2,5,6,9–12,15] Unlike the high prevalence rate of up to 90%,[12] none of our patients exhibited Brushfield's spots or iris hypoplasia. This can be explained by the dark-brown irises in our population. Wong and Ho also reported that none of the Hong Kong children showed these conditions either.[17] Wallis suggested that Brushfield spots

disappeared in blue-eyed infants whose irises subsequently turned brown.[15]

In summary, compared to Caucasian children with DS, Korean children with DS exhibited characteristic ocular findings which are composed of a previously unreported, high incidence of epiblepharon, the highest rate of exotropia and no cases of Brushfield spots or keratoconus. Unlike the non-DS children, the epiblepharon persists in DS children of older age, therefore slit lamp examination after the instillation of fluorescein should be performed in every Asian patient with DS. The difference in the incidence of ocular abnormalities according to race and age should be considered in every patient with DS.

## Acknowledgements

The authors have no proprietary interest in any of the products discussed in this article.

## References

1 Jones KL. Down syndrome. A. Chromosomal abnormality syndromes: In: Jones KL (ed). *Smith's Recognizable Patterns of Human Malformation*, 5th edn. Saunders: Philadelphia, 1997, pp 8–13.
2 Berk AT, Saatci AO, Ercal MD *et al*. Ocular findings in 55 patients with Down's syndrome. *Ophthalmic Genet* 1996; **17**: 15–9.
3 Solomons G, Zellwegger H, Jahnke PG, Opitz E. Four common eye signs in mongolism. *Am J Dis Child* 1965; **110**: 46–50.
4 Caputo AR, Wagner RS, Reynolds DR *et al*. Down syndrome. Clinical review of ocular features. *Clin Pediatr (Phila)* 1989; **28**: 355–358.
5 Jaeger EA. Ocular findings in Down's syndrome. *Trans Am Ophthalmol Soc* 1980; **78**: 808–845.
6 da Cunha RP, Moreira JB. Ocular findings in Down's syndrome. *Am J Ophthalmol* 1996; **122**: 236–244.
7 Hiles DA, Hoyme SH, McFarlane F. Down's syndrome and strabismus. *Am Orthopt J* 1974; **24**: 63–68.
8 Wagner RS, Caputo AR, Reynolds RD. Nystagmus in Down's syndrome. *Ophthalmology* 1990; **97**: 1439–1444.
9 Eissler R, Longenecker LP. The common eye findings in mongolism. *Am J Ophthalmol* 1962; **54**: 398–406.
10 Roizen NJ, Mets MB, Blondis TA. Ophthalmic disorders in children with Down syndrome. *Dev Med Child Neurol* 1994; **36**: 594–600.
11 Shapiro MB, France TD. The ocular features of Down's syndrome. *Am J Ophthalmol* 1985; **99**: 659–663.
12 Lowe RF. The eyes in mongolism. *Br J Ophthalmol* 1949; **33**: 131–154.
13 Igersheimer J. The relationships of lenticular changes in mongolism. *Trans Am Ophthalmol Soc* 1951; **45**: 595–624.
14 Doyle SJ, Bullock J, Gray C, Spencer A, Cunningham C. Emmetropisation, axial length, and corneal topography in teenagers with Down's syndrome. *Br J Ophthalmol* 1998; **82**: 793–796.
15 Wallis HRE. The significance of Brushfield's spots in the diagnosis of mongolism in infancy. *Arch Dis Child* 1951; **26**: 495.
16 Wagner HR. Mongolism in Orientals. *Am J Dis Child* 1962; **103**: 706–714.
17 Wong V, Ho D. Ocular abnormalities in Down syndrome: an analysis of 140 Chinese children. *Pediatr Neurol* 1997; **16**: 311–314.
18 Noda S, Hayasaka S, Setogawa T. Epiblepharon with inverted eyelashes in Japanese children. I. Incidence and symptoms. *Br J Ophthalmol* 1989; **73**: 126–127.
19 Jenkins RH. Demographics: geographic variations in the prevalence and management of exotropia. *Am Orthopt J* 1992; **42**: 82–87.