Ocular findings in Malaysian children with Down syndrome

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Abstract

Introduction: Down syndrome was first described as Mongoloid children with European parentage. Although their facial features resemble Orientals or Asians, ocular findings have not been well-documented in Asians, especially Malaysians. Our aim was to identify the ocular findings of Malaysian children with Down syndrome.

Methods: A total of 60 children with Down syndrome, aged between one month and 17 years, were examined for ocular findings from January 1995 to January 2004. Ocular examination, which includes visual acuity assessment, slit lamp biomicroscopy, ocular motility, cycloplegic refraction and ophthalmoscopy were performed whenever possible.

Results: The ocular findings include epicanthic fold in 96.7 percent (58), nystagmus in 33.3 percent (20), and strabismus in 26.7 percent (16) of children with Down syndrome, all of whom were esotropic. Other findings were bilateral congenital cataract in 13.3 percent (8), blepharoconjunctivitis in 10.0 percent (6), eyelid abnormalities in 6.7 percent (4), glaucoma in 6.7 percent (4), nasolacrimal duct obstruction in 3.3 percent (2), bilateral retinoblastoma in 1.7 percent (1), bilateral retinal detachment in 1.7 percent (1), and chronic uveitis in 1.7 percent (1) of children. Visual assessment showed that 47.3 percent of patients achieved good vision (6/12 to 6/6). Cycloplegic refraction was done in 24 patients (41.7 percent). Out of the 24 patients, 29.2 percent (7) were myopic, 25.0 percent (6) were hyperopic, and astigmatism was observed in 8.3 percent (2).

Conclusion: Malaysian children with Down syndrome demonstrated high incidences of epicanthic fold, nystagmus, and strabismus, and absence of Brushfield spots or keratoconus, which are in contrast to the ocular findings in Caucasian patients with Down syndrome. Rare ocular findings, such as bilateral retinoblastoma and retinal detachment, were also observed but their association with Down syndrome is not well-established.

Keywords: Down syndrome, epicanthic fold, eye manifestations, nystagmus, ocular lesions

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INTRODUCTION

In 1866, John Langdon Down described Down syndrome on the basis of an incorrect theory of racial regression[1]. He described these patients as having features similar to Mongol children but with European parentage. Evolution of medicine over the years has identified an abnormal chromosome composition responsible for their unique character[2]. Trisomy 21 was found to be the most common type followed by translocation and mosaicism. Most of the previous reports on the clinical features of Down syndrome have been on Caucasians. Reports on Asians with Down syndrome[3,4] showed different clinical features, especially in their ocular manifestations. Multiethnicity among Asians may further diverse the ocular manifestations of Down syndrome.

The incidence of Down syndrome in one of the largest government hospital in Malaysia was 1:959[5]. The highest incidence was reported among the Malays 1:981, followed by the Chinese 1:940 and Indians 1:860. Our hospital-based incidence was lower compared to the Western population. However, no previous observation on the ocular manifestations has been documented on Down syndrome children in Malaysia. Kelantan is a state situated at the northeast of Malaysia, bordering Thailand, and the majority of local populations are Malays. Hospital Universiti Sains Malaysia and Hospital Kota Bharu are two tertiary centres for the state. The objective

of our study was to identify the ocular features of Down syndrome children in our local population.

METHODS

Clinical reviews and prospective data collection were conducted involving Down syndrome patients seen in the eye clinic of Hospital Universiti Sains Malaysia and Hospital Kota Bharu, Kelantan, from January 1995 to January 2004. A total of 60 children with Down syndrome were enrolled into this study. The first part of the study involved 25 Down syndrome children, obtained through retrospective review of medical records. The second part involved 19 patients, who were seen in the eye clinic of the above hospitals from January 2003 to January 2004. 16 patients were recruited through community eye services conducted at Kota Bharu Lion's Club Down Syndrome Centre in June 2003. The Kota Bharu Lion's Club Down Syndrome Centre, a non-governmental organisation, provides early intervention programmes for Down syndrome children aged from three to six years of age.

The diagnosis of Down syndrome was made either on cytogenetic analysis or by clinical characteristics. Parents of all these children originated from Kelantan, as confirmed by the Kelantan state code in their identity cards. Demographical data was recorded, which included the age at their first visit to the eye clinic, source of referral, ethnicity, sex, family history of Down syndrome and social status of the parent. Any information or examination, that was not recorded or carried out was classified as undetermined data. Ocular examination, including visual acuity assessment, slit lamp biomicroscopy, ocular motility, cycloplegic refraction and ophthalmoscopy, were performed on all cooperative children. Visual acuity assessment was performed by various methods according to the abilities of the respective child. These include Snellen chart, Sheridan Gardner and Catford drums. Other methods include perception to light, small toys and blinking reflex.

Cycloplegic refraction was done when possible, depending on cooperativeness of the children. Myopia was defined as refractive error as more than -0.50 spherical equivalent, hyperopia as more than +0.50 spherical equivalent, and astigmatism as greater than 0.50 dioptre of cylinder according to the age of the children. Slit lamp biomicroscopy was only performed on cooperative children more than 12 months old. Eyelid margin, conjunctiva, abnormalities of the cornea, iris and lens were examined. The findings of the uncooperative children and those less than 12 months of age were based on torchlight examination. The posterior segment was visualised with binocular indirect ophthalmoscope. Uncooperative children were either given oral chloral hydrate (25mg/kg) or examined under anaesthesia.

Placido disc was used to detect keratoconus. Strabismus assessment was performed if the eye was not orthophoric on Hirschberg test. Nasolacrimal duct obstruction was diagnosed based on history of epiphora or recurrent mucopurulent discharge. Examination under anaesthesia was conducted to confirm the diagnosis, whereby syringing and other examinations to rule out other causes of epiphora were performed.

Table I. Demographical data.

Variable	
Age (Mean ±SD)	6.72 ± 3.38 years
Age at first visit (Mean ± SD)	3.96 ± 3.48 years
Sex	
Male	26 (43.3%)
Female	34 (56.7%)
Race	
Malay	56 (93.3%)
Chinese	3 (5.0%)
Indian	1 (1.7%)
Others	–
Positive family history	2 (3.3%)
Reason for eye clinic consultation	
Completion of special school form	4 (6.6%)
Referral from paediatric clinic	24 (40.0%)
Referred for ocular problem	16 (26.7%)
Community eye service	16 (26.7%)
Confirmation of diagnosis	
Cytogenetics study	7 (4.7%)
Clinical features	53 (88.3%)

Table II. Visual acuity assessment methods.

Methods	
Snellen chart	2 (3.3%)
Sheridan Gardner chart	6 (10.0%)
Catford drum	23 (38.3%)
Beads	2 (3.3%)
Others	8 (13.3%)
Undetermined	19 (31.7%)
Total	60 (100%)

Table III. Visual acuity.

	OD (n=60)	OS (n=60)	Better eye's best corrected visual acuity (n=60)
6/6 – 6/12	24 (40.0%)	26 (43.3%)	26 (43.3%)
6/18 – 6/60	12 (19.9%)	7 (11.7%)	10 (16.7%)
Counting finger or worse	1 (1.7%)	3 (5.0%)	1 (1.7%)
Perception to light	7 (11.7%)	7 (11.7%)	7 (11.7%)
Undetermined	16 (26.7%)	17 (28.3%)	16 (26.7%)

RESULTS

The majority of these children had their diagnosis of Down syndrome made based on their clinical features (Table I). Only seven patients agreed to undergo cytogenetics analysis. 93% of these children were Malays, 5.0% Chinese and 1.7% (one) was Indian. This ethnic distribution reflects the local ethnic composition of the state of Kelantan. 56% of these children were female and 43.3% were male. The majority was referred from the paediatric clinic. Their mean age at first visit to the eye clinic was 3.96±3.48 years. The mean age for the overall study groups (Table I) was calculated based on the age of their last visit to the eye clinic for the retrospective group and age at first visit for the prospective group (6.72±3.38 years old). Only two children had a positive family history of Down syndrome.

Various methods were used to assess the visual acuity of the Down syndrome children (Table II). Catford drum (38.3%) was the most common tool used. Those without any record on visual testing, as well as those whose visual acuity assessments could not be carried out, were grouped under "undetermined". "Others" include perception to visual sensation such as toys, blinking reflexes and light. Snellen chart visual acuity assessment was only successfully performed on two children (Table II). 43.3% of these children achieved good vision in at least one eye (Table III). Cycloplegic refraction was successfully performed on 25 children (Table IV). One aphakic child was excluded. There was an equal percentage of hyperopia and myopia for children less than ten years old. Only two children were diagnosed as having only astigmatism. Nine other children were considered emmetropic.

The most consistent ocular finding was the presence of the prominent epicanthic fold (96.7%) (Table V). Nystagmus was observed in 33.3% (20) of Down syndrome children. Strabismus was observed in 16 children and all of them were esotropic.

Table IV. Refractive error.

Age (years)	Myopic (range power)	Hyperopic (range power)	Astigmatism (range power)
0 to <5	4 (0.5-7.0D)	4 (3.5-4.25D)	–
5 to <10	2 (1.5-6.5D)	2 (4.0-4.5D)	1 (6.0D)
10 to <15	1 (6.5D)		1 (3.0D)
Total	7 (29.2%)	6 (25.0%)	2 (8.3%)

Table V. Ocular manifestations.

Ocular manifestation	n=60
Nystagmus	20 (33.3%)
Strabismus	
Esotropia	16 (26.7%)
Exotropia	–
Eyelids abnormalities	
Prominent epicanthic fold	58 (96.7%)
Entropion	1 (1.7%)
Ectropion	–
Epiblepharon	1 (1.7%)
Ptosis	2 (3.3%)
Chalazion	2 (3.3%)
Stye	2 (3.3%)
Blepharitis	6 (10.0%)
Conjunctivitis	4 (6.7%)
Brushfield spots	–
Keratoconus	–
Nasolacrimal duct obstruction	2 (3.3%)
Cataract	
Congenital	8 (13.3%)
Developmental	–
Secondary	–
Glaucoma	4 (6.7%)
Retinal detachment (bilateral)	1 (1.7%)
Retinoblastoma (bilateral)	1(1.7%)
Chronic uveitis (bilateral)	1 (1.7%)

Other eyelids abnormalities included entropion, epiblepharon and ptosis. We also observed the presence of eyelid infection, which included stye, chalazion and blepharoconjunctivitis. Other findings included cataract (13.3%), glaucoma (6.7%), nasolacrimal duct obstruction (3.3%), bilateral retinoblastoma (1.7%), bilateral retinal detachment (1.7%) and chronic uveitis (1.7%).

DISCUSSION

Prominent epicanthic fold is the most consistent ocular manifestation in our study population. Similar findings were also observed among Chinese Down syndrome children in Hong Kong[3] and Korea[4]. Perhaps the unique eyelid structures of Asians made the abnormalities of eyelids in these children more pronounced. Benda[6] observed that epicanthic folds in children with Down syndrome regressed slower compared to normal children, though the prevalence decreased with older age. Perhaps, a comparative, age-matched study between Down syndrome children and normal children will give a better understanding of the eyelids abnormalities.

Upward slanting of the palpebral fissure was another common finding among the Chinese[3,4]. We conducted the assessment of palpebral fissure slant on two groups only: the prospective group and during community eye screening using a similar modified protractor devise created by Shapiro and France[7]. We were unable to document the upward slanting of the palpebral fissure involving children in the retrospective group. As we did not have any age-matched controls for the palpebral fissure slant measurement, and there is no baseline data for Malaysian children, we were unable to provide accurate data on the abnormal position of the palpebral fissure.

Epiblepharon was only detected on one child. Though epiblepharon is generally common among Asians, it tends to resolve with facial growth[8]. The mean age of our Down syndrome children in our study was 6.72±3.38 years old, which was within the age that the epiblepharon had already resolved. The other possibility may be due to the association with the type of chromosomal abnormalities. Unfortunately, only seven of our children were diagnosed based on cytogenetic analysis, therefore, we were not able to relate these findings. The difficulty in obtaining consent for cytogenetic analyses as well as tracing the children for the analysis were the major contributing factors to our failure in establishing the cytogenetic diagnosis. However, we were confident with our clinical diagnosis.

The combination of abnormal skin of Down syndrome children[9] and impairment of their immune response system[10] may be responsible for their susceptibility to eyelid infection. We reported two cases of chalazion, two cases of stye and six cases of blepharoconjunctivitis. The higher incidence of the eyelid infection in our study was most likely because the majority of the children was referred for eye problems. Most probably for the same reason, we reported a high incidence of nystagmus among our Down syndrome children. Perhaps, a future study involving children seen during community eye screening will give a more accurate incidence of the ocular findings in our local Down syndrome children.

20 of our Down syndrome children (33.3%) presented with nystagmus, which was higher than previous studies[11,12]. To our knowledge, we reported the highest incidence of nystagmus. However, despite the high incidence of nystagmus, about 40% achieved good vision bilaterally. Unfortunately, we failed to determine the specific type of nystagmus as described by Wagner et al[12]. He observed that the nystagmus in Down syndrome patients is not always associated with significant decreased visual acuity and was not indicative of severe ocular abnormalities or structural neurological diseases. Interestingly, he also reported the high incidence of esotropia among Down syndrome patients with nystagmus but failed to establish any correlation of both abnormalities. Similarly, 26.7% of our study population presented with strabismus, and all were esotropic.

Despite the high incidence of nystagmus, the incidence of cataract in our children was almost similar with other study populations[3,7,18]. All with congenital cataract were detected within the first six months of life, except for two cases (detected at the age of six and 11 years, respectively). Cataract is mostly detected in children above 12 years old among Caucasians with Down syndrome[19,22]. The mean age of the first visit to our clinic was 3.96±3.48 years, which was alarming. Late detection of cataract may lead to late intervention resulting in amblyopia and even blindness.

A major weakness in our study was the large number of undetermined visual acuity. We were only able to assess two children using the Snellen chart. The Catford drum, the commonest tool used in our visual assessment, is the least accurate, especially in normal children with nystagmus. The eye movements may be influenced by the sound produced by the rotating drum rather than the ability

to see the target. Smaller moving targets can be seen in comparison to a stationary target of similar size, requiring steady fixation. The Catford drum tends to overestimate visual acuity by a factor of four[13] and is more useful in comparing the behaviour of one eye with that of the other. Perhaps, a better method of assessment should have been conducted to provide accurate documentation of visual ability among Down syndrome children in our population.

Failure of emmetropisation among Down syndrome children is believed to cause high incidence of refractive error[14]. Hyperopia was found to be more common than myopia in most observations[3,4,14,15]. In our study, cycloplegic refraction was performed on only 25 cooperative children and only 24 children were included. We reported a slightly higher percentage of myopia compared to hyperopia. However, due to a small number of successful cycloplegic refractions performed in our study, we were unable to conclude the commoner type of refractive error. Based on the biometry study, thinning of the cornea stroma may have resulted in steeper cornea and reduced corneal rigidity, which may in turn be responsible in a high incidence of astigmatism and believed to play an important aetiological factor for keratoconus[15].

Oblique astigmatism, with striking right and left specificity, has been found to be the commonest type of astigmatism among Caucasian Down syndrome children[14,15]. The specific 135 degrees axis astigmatism of right eyes and 45 degrees axis of left eye may be due to the effect of upward slanting of palpebral fissure to the cornea. In spite of the absence of keratoconus, 31% of Korean Down syndrome children were found to be astigmatic[4], though the specific observation of the type of astigmatism was not made. However, in our population with majority of Malay children, the incidence was much lower.

Occurrence of glaucoma in Down syndrome was rather rare[16]. We recorded four cases of glaucoma; consisting of two cases of infantile glaucoma, one case of glaucoma suspect (not fully worked up yet) and one case of secondary glaucoma. Though intraocular pressure was not performed on all children in our study, glaucoma needs to be excluded especially in children with epiphora[17]. Secondary glaucoma in our study was due to bilateral chronic uveitis, which has not been reported in Down syndrome children.

Although Down syndrome children were believed to be more susceptible to develop retinoblastoma, the incidence is quite infrequent[20,21]. 15 cases have been reported[21], which suggests the possible association of Down syndrome and retinoblastoma. We recorded one patient with bilateral retinoblastoma, which was thought to be hereditary retinoblastoma. She defaulted on follow-up for a year after the diagnosis was made and presented again with extraocular involvement. Unfortunately, she died after two years of treatment. Late presentation and high default rate among our local children with retinoblastoma lead to difficulty in differentiating hereditary and sporadic retinoblastoma. A majority of them presented with advanced retinoblastoma and extraocular extension, leading to a poor survival rate.

We also reported one case of bilateral retinal detachment without any history of trauma. Previous reports have linked the retinal detachment to trauma and retinal dialysis[17,19,23]. Unfortunately we did not document the other fundus details in this study. The presence of Brushfield spots or specks on the iris is believed to be a pathognomonic feature of Down syndrome. However, this observation was based on Caucasian populations. Later, as more observations were carried out among other races, Brushfield spots were detected more frequently in light-coloured irides[18]. Brushfield spots were absent on the irides of all the Down syndrome children in our population. Similar observation was also noted among the Chinese children[3,4]. However, slit lamp biomicroscopy was performed on only 15 children in our study, which may result in underdetection of iris abnormalities. da Cunha and Moreira[19] observed the presence of Brushfield's spots and hypoplasia of the iris in only 52% of their study population in spite of a 95% slit lamp biomicroscopy usage. They postulated that the lower prevalence in their study was due to high incidence of dark irides (108 children with dark-coloured irides out of 152 total samples) in their population. They also observed that in light-coloured irides, the iris anomalies were detected in up to 98% as compared to only 33% in dark-coloured irides.

Keratoconus was detected in up to 15%[7,18] in other populations with increasing prevalence in the older age group but was not observed in our Down syndrome children. However, there has been no established evidence to link genetic abnormality of Down syndrome to keratoconus. It is thought to be due to eye rubbing or underlying structural abnormalities of the cornea[15]. In spite of the exhaustive list of ocular findings, we believe the most important findings were those that are treatable, such as cataract, refractive error, strabismus and cataract. Perhaps, a better referral and screening

system should be implemented to avoid blindness and amblyopia in our set-up. Down syndrome children should be screened for ocular abnormalities within the first three months of life and later, annually. Improvement in vision will help to increase the quality of life of our Down syndrome children.

In conclusion, Malaysian children with Down syndrome demonstrated a high incidence of epicanthic fold, nystagmus, strabismus and cataract. We noted a prominent absence of Brushfield spots or keratoconus, which was in contrast to the ocular findings in Caucasian patients with Down syndrome. Rare ocular findings, such as bilateral retinoblastoma, uveitis and retinal detachment, were also observed but their association to Down syndrome is not well established.

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