RESEARCH REPORT

Strabismus, refractive errors and nystagmus in children and young adults with Down syndrome

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ABSTRACT

Purpose: The aims of the present population-based, cross-sectional study were to examine the frequency and type of strabismus, refractive errors and nystagmus in children and young adults with Down syndrome (DS) in Macedonia and Croatia.

Methods: A total of 170 unselected children and young adults with DS aged 1–34 years were examined for ocular findings. The ocular examination included: a visual acuity assessment, cycloplegic refraction, ocular alignment and ocular motility.

Results: Strabismus was found in 45 of 170 children (26.5%), and esodeviation was the most common type. Nine (20%) had exodeviation and 4 (8.9%) vertical deviation. In 27 of 32 esotropic patients, the strabismus was regarded as acquired esodeviations. The frequency of strabismus was lowest in the high-grade hyperopia group (5%). Concerning esodeviations, fewer cases (3%) were in the high-grade hyperopia group. Most of the cases with esodeviations were in correlation with low-grade hyperopia (31%), myopia (28 %) and emetropia (16%). Hyperopia was the most common refractive error and high myopia increased in prevalence in the over 20 age group. Astigmatism was present in 72.4% of patients. Nystagmus was observed in 18 patients. Ten of 18 patients with nystagmus were associated with the presence of strabismus (9 esodeviations, 1 exotropia).

Conclusion: In our study, the high prevalence of strabismus can not be attributed to the presence of hyperopia. Our data show no association between refraction and strabismus in children with DS. Oblique astigmatism has been found to be the most common type of astigmatism in our study group.

Keywords: Down syndrome, strabismus, refractive errors, nystagmus, amblyopia

INTRODUCTION

Strabismus and refractive errors are frequently encountered in Down syndrome (DS).¹⁻³ Various studies on non-selected populations of individuals with DS have reported a prevalence of strabismus of 20–42%.¹⁻⁴⁻⁷ Two studies found the prevalence of strabismus to be less than 20%.⁸⁻⁹ Strabismus and refractive errors are frequently encountered in Down syndrome (DS).¹⁻³ Various studies on non-selected populations of individuals with DS have reported a prevalence of strabismus of 20–42%.¹⁻⁴⁻⁷ Two studies found the prevalence of strabismus to be less than 20%.⁸⁻⁹

There are several studies reporting refractive errors in 30–51% of DS patients.²⁻³,⁸⁻¹⁰ Frequency of nystagmus in the Down population in different studies is 8–30%.¹¹⁻¹⁴ Concerning amblyopia, the reported frequency in different studies is 8.5–26%.⁵⁻¹²⁻¹⁴⁻¹⁵ The aim of the present population-based, cross-sectional study was to examine the prevalence of strabismus, refractive errors, nystagmus and amblyopia in children and young adults with DS.

SUBJECTS AND METHODS

Non-selected home reared children and young adults with DS enrolled in this population-based, cross-sectional study, were recruited from the special educational system, social services as well as parental associations in the region of Macedonia and Croatia.

A total of 170 children and young adults with DS who were enrolled were seen in the private polyclinic “Medika plus” in the capital Skopje, Macedonia, in the private polyclinic “Svjetlost” in the capital Zagreb, Croatia, as well as in local private eye offices in eight other towns, in Macedonia and in one other town in Croatia. The study was performed in the period from March 2007 until July 2009.

The diagnosis of DS was made either on clinical characteristics or by cytogenetic analysis. All parents...
of Macedonian children originated from Macedonia, except two mothers from Bulgaria, and the Croatian children all originated from Croatia. Written informed consent was obtained from each subject’s parent.

All subjects (98 male, 72 female) between 1 year and 34 years of age were examined for ocular findings by one of the authors (A.Lj.). Protocols for general health, birth dates and ocular examination which included a visual acuity assessment, cycloplegic refraction, ocular alignment and motility were prepared.

**Eye Alignment**

The alignment of the eyes was a standard evaluated for distance fixation using Hirschberg’s corneal reflex method, and cover test. The cover test was also performed using an accommodative fixation target. Both distance and near ocular alignment were tested with optical correction, if prescribed. Examination of the motility was done in subjects who were cooperating. Deviation from the straight position was classified as esodeviations, exodeviations or vertical deviations. In addition, the deviations were classified into unilateral or alternating strabismus, and it was noted whether the deviation was manifest or intermittent.

Infantile esodeviations were defined as a constant esodeviation with an onset before 6 months of age reported by the mother. All other cases of esodeviations were classified as acquired esodeviations. These were divided according to refractive error into hyperopic, myopic, and anisometropic groups. Microtropia was defined as a deviation of less than 10 prism diopters. Intermittent exotropia and manifest exotropia were designated as an exodeviation. The presence of nystagmus was noted (latent or manifest).

**Visual Acuity and Refraction**

In cooperative children and young adults, the best corrected visual acuity was tested with full line Snellen visual acuity charts in the better eye. In Macedonia and Croatia there is no use of charts for accurate assessment of children and adults with intellectual disability.

Amblyopia was defined as a difference in visual acuity between the two eyes of more than one line on the acuity chart.

Cycloplegic refraction was performed after three to five installations of one drop of Cyclopentolate 1%. In this study we used photorefraction (Auto-Ref-Keratometer Potec PRK-5000).

For each of the subjects, spherical equivalent and power and axis of cylinder were recorded. 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.

Low grade hyperopia was defined as +1.00 D to +2.75 D spherical equivalent, moderate hyperopia as +3.00 D to +5.75 D spherical equivalent and high-grade hyperopia as ≥ +6.00 D spherical equivalent. Respectively, myopia was divided into low-grade, moderate and high-grade myopia.

Anisometropia was defined as the difference between the right and the left eye > 1.0 spherical and/or >1.50 cylinder power

Clinically significant astigmatism was defined as refractive error ≥1.0 D of the cylinder. In the evaluation of astigmatism group, minus form of the cylinder was used.

The axis of astigmatism was classified as follows: WTR (“with the rule”), ATR (“against the rule”) and OBL (oblique astigmatism or axis between 100–170 and 10–80). Eyes with a cylindrical power of < 1.0 D were excluded from the astigmatism group (Table 1).

**Statistical Analysis**

The data were analyzed statistically with the SPSS for Windows version 13.0, using χ² test and Fisher’s exact test, and P<0.05 was chosen as the level of statistical significance.

**RESULTS**

The mean age of the patients was 13.8 years (range 1–34 years). The age distribution of all subjects is given in Fig. 1. The mean maternal age at birth of the children was 29.1 years. In our study population 98 (57.9%) of the examined children and young adults with DS were male, 42.1% female. All the DS patients were Caucasian.

Regarding ethnicity, 48.5% were Macedonians, 37.4% Croatians, 13.5% Albanians and 0.6% Roma.

| **Table 1. Astigmatism in children and young adults with DS.** |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Author**      | **Year**        | **Method of refraction** | **No of patients** | **Astigmatism ≥ 1.0 D** | **WTR** | **ATR** | **OBL** |
| Woodhouse²      | 1997            | Non-cycloplegic       | 24 (4y–12y)       | 37.5%            | Axis not reported |
| Haugen³         | 2001            | Cycloplegic           | 60 (2.5y–11y)     | 57%              | 68%            | 6%              | 26%              |
| Doyle¹⁸         | 1998            | Cycloplegic           | 50 (15y–22y)      | Not reported     | 22%            | 39%            | 38%              |
| Present study   | 2010            | Cycloplegic           | 145 (1y–34y)      | 72.4%            | 37%            | 11%            | 52%              |

WTR, with the rule; ATR, against the rule; OBL, oblique astigmatism.
Strabismus in Down syndrome

Strabismus was found in 45 of 170 children (26.5%), and esodeviation was the most common type (32 of 45 children, 71.1%). Nine (20%) had exodeviation and four (8.9%) vertical deviation (hypertropia).

In 28 of 32 esotropic patients the strabismus was regarded as an acquired esodeviation, four were classified as an infantile esodeviation. In nine cases with exodeviation, two were found to have intermittent exotropia and seven manifest exotropia. One patient with manifest exotropia had Brown syndrome. Three patients with acquired esodeviations had A syndrome.

Table 2 shows the presence of strabismus (all and separate esodeviations) in different groups of spherical equivalent refractive errors. The frequency of strabismus was lowest in the high-grade hyperopia group (5%). Concerning esodeviations, fewer cases were found in the high-grade hyperopia group. Most of the cases with esodeviations were in correlation with myopia and emmetropia and the low-grade hyperopia refractive group.

### Table 2: Prevalence of strabismus (all types) and specifically esodeviations (Italic numbers in brackets) in 170 children and young adults with DS, classified by refractive state in spherical equivalent.

<table>
<thead>
<tr>
<th>Refractive state</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 Myopia</td>
<td>12(9)</td>
<td>26(30)</td>
</tr>
<tr>
<td>Group 2a Emmetropia</td>
<td>7(5)</td>
<td>16(16)</td>
</tr>
<tr>
<td>Group 2b Low grade hyperopia</td>
<td>10(10)</td>
<td>22(31)</td>
</tr>
<tr>
<td>Group 2c Moderate hyperopia</td>
<td>8(2)</td>
<td>17(7)</td>
</tr>
<tr>
<td>Group 2d High grade hyperopia</td>
<td>2(1)</td>
<td>5(3)</td>
</tr>
<tr>
<td>Group 3 Anisometropia</td>
<td>3(3)</td>
<td>7(10)</td>
</tr>
<tr>
<td>Group 4 No refractive state provided</td>
<td>3(2)</td>
<td>7(3)</td>
</tr>
<tr>
<td>Total</td>
<td>45(32)</td>
<td>100(100)</td>
</tr>
</tbody>
</table>

### Table 3: Classification of esodeviations in 32 children and young adults with DS.

<table>
<thead>
<tr>
<th>Type of esodeviations</th>
<th>Subjects, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infantile</td>
<td>4</td>
</tr>
<tr>
<td>Associated with emetropia</td>
<td>4</td>
</tr>
<tr>
<td>Acquired</td>
<td>28</td>
</tr>
<tr>
<td>Associated with hyperopia</td>
<td>13</td>
</tr>
<tr>
<td>Associated with myopia</td>
<td>9</td>
</tr>
<tr>
<td>Associated with anisometropia</td>
<td>3</td>
</tr>
<tr>
<td>Associated with emetropia</td>
<td>1</td>
</tr>
<tr>
<td>No refractive state provided</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
</tr>
</tbody>
</table>

Classification of the esodeviations in 32 children and young adults with DS is presented in Table 3.

The patients with acquired esodeviations associated with hyperopia were classified as: nonaccommodative esodeviations (n = 10), partially accommodative (n = 2) and one patient had refractive accommodative esodeviations (n = 1). Only one patient had convergence excess.

Concerning astigmatism and strabismus, 31% of the strabismus patients showed the presence of clinically significant astigmatism. In three strabismic patients, the refractive state was not provided.

Two patients with intermittent exotropia had low-grade myopia and low-grade hyperopia. Seven patients with alternate exotropia had all mostly moderate grade hyperopia. In one patient with alternate exotropia, no refractive status was provided.

The age of the nine subjects with exodeviations is shown in Table 4. The age of 32 subjects with esodeviations is shown in Table 5. The mean age of the esodeviation group was 17.6 ± 8.48 years and the esodeviation group had a mean age of 14.1 ± 7.36. There was no statistical difference in age between the two groups (P = 0.23).

Concerning the four patients with vertical strabismus (all hypertropia), one had moderate hyperopia, while the other patient had high grade myopia. In one
patient with vertical strabismus, no refractive status was provided.

**Refractive errors**

Of the 170 individuals, 25 did not co-operate well. The age distribution of 145 subjects, where refractive error was analyzed is given in Fig. 2. The refractive state (spherical equivalent) showed emmetropia 35 (24.1%), more hyperopia 80 (55.2%) and myopia 30 (20.7%) (Fig. 3). In the present study, 5 of 30 subjects with myopia have snow-flake opacities and one has keratoconus. Most of the myopic patients were in the range ≥ −6.0 D and aged ≥ 15 years (Fig. 4). The highest value of myopia was −22.0 D.

Hyperopia in this population was mostly within range power +1.00 D to +2.75 D and at the age ≥15 years (Fig. 5). Overall, hyperopia increases with age group. Astigmatism was present in 105 subjects of 145 (72.4%). The most prevalent form of astigmatism was oblique astigmatism 55/105 (52.4%) (Table 1). Astigmatism as a function of age is presented in Fig. 6 where the prevalence of oblique astigmatism is seen to gradually increase with the age of the subjects.

A total of 25% of the children and young adults with DS were corrected before the study but 36% of subjects needed a correction and did not have one at the time of the study.

Full hyperopic correction has been prescribed to all hyperopic patients with esodeviations exceeding 2.50 D.

**Nystagmus**

Nystagmus was observed in 18 patients (11%) (16 manifest; 1 manifest-latent; 1 latent). Sixteen children had a horizontal jerk nystagmus, two had a pendulating nystagmus.

Ten of 18 patients with nystagmus, had high-grade myopia and seven had hyperopia. Five of 18 patients with nystagmus, also showed clinically significant astigmatism. Ten of 18 patients with nystagmus also showed strabismus (9 esodeviations, 1 exotropia). Most of the patients with nystagmus and strabismus had high-grade myopia. Refractive errors in the nystagmus group are shown in Fig. 7.

**Visual Acuity**

Of the 170 individuals with DS, 87 were unable to complete acuity testing. Visual acuity was evaluated in 83 (49%) children and young adults, using best correction and presented in decimal Snellen.

The frequency of amblyopia in 83 patients, who were able to complete acuity testing in our study, was 16.9%. The degrees of amblyopia in amblyopic subjects are presented in Table 6.
FIGURE 2  Age distribution of 145 subjects with DS for whom refractive errors were analyzed.

FIGURE 3  Refractive status (spherical equivalent) in 145 subjects with DS.

FIGURE 4  Myopia (spherical equivalent).

FIGURE 5  Hyperopia (spherical equivalent).
DISCUSSION

Although the presence of strabismus in DS may be predictive of a significant refractive error, a refractive error is not necessarily indicative of a strabismus. The association between strabismus and abnormal refractive development is unclear. Strabismus is a common finding in individuals with DS. The prevalence of strabismus in our study was 26.5% which is similar to a study by Tsirias who found a prevalence of 22% but lower than Haugen and Høvding who reported strabismus in all refractive groups among their cohort of children with DS with an overall prevalence of 42%, and Jaeger who found a prevalence of 41.3%.

Most authors have identified esodeviations. The prevalence of esodeviations in our strabismic DS population was 71.1%. Exodeviations were found in nine patients (20%) in this study, but it has been reported to be as low as 6%. Exodeviations in our study were most associated with hyperopia and were seen at ages from 7–25 years (Table 4).

Hyperdeviations have been uncommon and associated with A or V patterns, dissociated vertical deviation, Brown’s syndrome, or oculomotor nerve palsy. In this study, we observed four patients (8.9%) with hypertropia without these associations, similar to the prevalence rate of da Cunha and de Morreira.

The high prevalence of strabismus in the present study cannot be attributed to the presence of hyperopia. Our data show no association between refraction and strabismus in children with DS.

As other studies have shown, hyperopia is the most common refractive error in DS. The incidence of hyperopia (spherical equivalent) in this study was 55.2% and myopia (spherical equivalent) 20.7%. Haugen and Cregg showed that failure of emmetropization to occur is a characteristic of many children with DS. Doyle showed that axial length correlated with spherical equivalent. A linear association was found between axial length and spherical equivalent refraction.

However, reports show that although hyperopia is more common in individuals with myopia, the degree of myopia can be extremely high. In the present study, 12 of 145 subjects had myopia of −8.00 D or greater.

The incidence of astigmatism in the population with DS in Macedonia and Croatia was 72.4% which is higher

<table>
<thead>
<tr>
<th>Degree of amblyopia</th>
<th>Subjects, n</th>
<th>Subjects, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (2–4 rows difference)</td>
<td>12</td>
<td>85.7</td>
</tr>
<tr>
<td>Moderate (5–7 rows difference)</td>
<td>2</td>
<td>14.3</td>
</tr>
<tr>
<td>Profound (&gt; 7 rows difference)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>100</td>
</tr>
</tbody>
</table>

FIGURE 6 Astigmatism as a function of age. WTR, with the rule; ATR, against the rule.

FIGURE 7 Refractive errors in the nystagmus group.
with the general population. Association between snowflake lens opacities and keratoconus with high myopia in the older age group should be the object of further study. Screening, evaluation and treatment of ocular and refractive findings in children and young adults with DS is regularly needed.

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Declaration of interest: The author reports no conflicts of interest. The author alone is responsible for the content and writing of the paper.

REFERENCES

18. Doyle SJ, Bullock J, Gray C, Spencer A, Cunningham C. Emmetropisation, axial length, and corneal

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