

EXTENDED REPORT

Prevalence and associations of anisometropia and aniso-astigmatism in a population based sample of 6 year old children

S C Huynh, X Y Wang, J Ip, D Robaei, A Kifley, K A Rose, P Mitchell

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See end of article for authors' affiliations

Correspondence to:
Paul Mitchell, MD, PhD,
FRCOphth, Centre for
Vision Research,
Department of
Ophthalmology, University
of Sydney, Hawkesbury
Road, Westmead, NSW
2145, Australia;
paul_mitchell@wmi.usyd.
edu.au

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Aim: To study the distribution of anisometropia and aniso-astigmatism in young Australian children, together with clinical and ocular biometry relations.

Method: The Sydney Myopia Study examined 1765 predominantly 6 year old children from 34 randomly selected Sydney schools during 2003–4. Keratometry, cycloplegic autorefraction, and questionnaire data were collected.

Results: Spherical equivalent (SE) anisometropia (≥ 1 dioptre) prevalence was 1.6% (95% confidence interval (CI) 1.1% to 2.4%). Aniso-astigmatism (≥ 1 D) prevalence was 1.0% (CI: 0.6% to 1.6%). Both conditions were significantly more prevalent among moderately hyperopic (SE ≥ 2.0 D) than mildly hyperopic (SE 0.5–1.9D) children. Myopic children (SE ≤ -0.5 D) had higher anisometropia prevalence. Neither condition varied by age, sex, or ethnicity. In multivariate analyses, anisometropia was significantly associated with amblyopia, odds ratio (OR) 29, (CI: 8.7 to 99), exotropia (OR 7.7, CI: 1.2 to 50), and neonatal intensive care unit (NICU) admission (OR 3.6, CI: 1.1 to 12.6). Aniso-astigmatism was significantly associated with amblyopia (OR 8.2, CI: 1.4 to 47), maternal age >35 years (OR 4.0, CI: 1.3 to 11.9), and NICU admission (OR 4.6, CI: 1.2 to 17.2). Anisometropia resulted from relatively large interocular differences in axial length ($p < 0.0001$) and anterior chamber depth ($p = 0.0009$). Aniso-astigmatism resulted from differences in corneal astigmatism ($p < 0.0001$).

Conclusion: In this predominantly 6 year old population, anisometropia and aniso-astigmatism were uncommon, had important birth and biometry associations, and were strongly related to amblyopia and strabismus.

Anisometropia, an interocular difference in refraction, is an important condition in children because it can lead to significant visual problems, including aniseikonia and impaired stereopsis,¹ amblyopia,² and strabismus.³ It occurs despite both eyes being under similar environmental influences. Knowledge of its prevalence, associated factors, and relation to ocular biometry will help to further understand development of this and other refractive errors.

While associations with prematurity and low birth weight have been examined in non-population based studies,^{4–6} associations with parental characteristics and other child related factors are not known. Various maternal factors have been found to increase the risk for childhood conditions, including increasing maternal age and congenital malformations,⁷ smoking and strabismus,⁸ and breast feeding and myopia.⁹ It is not known if anisometropia and aniso-astigmatism are associated with these maternal factors. Further, associations with other measures of development at birth such as birth length and head circumference have not previously been explored. Earlier studies also used relatively small,^{10–11} selected samples^{12–14} or adults,^{15–16} and many ignored astigmatic anisometropia.^{10–14, 17–18}

In this study, we aimed to: (1) study prevalence of anisometropia and aniso-astigmatism; and (2) explore associations with parental characteristics, childhood parameters and ocular biometry, in a population based sample of predominantly 6 year old children.

PATIENTS AND METHODS

Subjects

The Sydney Myopia Study is a population based study of eye health in Australian schoolchildren. It was approved by the

University of Sydney human research ethics committee and Department of Education and Training (Sydney, Australia). Detailed study methods are described elsewhere.¹⁹ Informed consent was obtained from parents. Six year old children were recruited during 2003–4 from 34 primary schools using random cluster sampling.

Ocular measurements

Ocular biometry was performed using the IOLMaster (Carl Zeiss, Germany). Axial length (AL) was measured from the anterior corneal surface to retinal pigment epithelium along the visual axis.²⁰ Anterior chamber depth (ACD) was measured after cycloplegia to minimise accommodative variability. Five valid measures of axial length and anterior chamber depth, and three keratometry measures, were obtained.

Cycloplegia was induced with 1% cyclopentolate and 1% tropicamide, following 1% amethocaine. Five autorefractions were performed (RK-F1 autorefractor-keratometer, Canon, Japan) 30 minutes later.

Questionnaire data

Questionnaires (193 item) completed by parents provided information on parental age at the child's birth, smoking during pregnancy (active, passive), and breastfeeding. Child related factors included ethnicity, neonatal intensive care unit (NICU) admission, multiple birth, developmental delay,

Abbreviations: ACD, anterior chamber depth; AL, axial length; NICU, neonatal intensive care unit; RA, refractive astigmatism; SE, spherical equivalent; VA, visual acuity

Table 1 Prevalence of spherical equivalent (SE) anisometropia of at least 1.0D stratified by sex, ethnicity, and worse eye refraction, with 95% confidence intervals (CI)

	Number of children (%)	Prevalence (n = 28)	
		%	95% CI
All	1724 (100.0)	1.6	1.1 to 2.4
Girls	849 (49.3)	2.1	1.3 to 3.4*
Boys	875 (50.7)	1.1	0.6 to 2.1
Ethnicity†			
European white	1096 (63.6)	1.6	1.0 to 2.6*
East Asian	295 (17.1)	2.4	1.1 to 5.0
Worse eye refraction‡			
Moderate hyperopia	228 (13.2)	10.1	6.7 to 15.2§
Mild hyperopia	1384 (80.3)	0.1	0.04 to 0.6
Emmetropia	86 (5.0)	0	–
Myopia	26 (1.5)	11.5	3.7 to 35.8§

*No significant sex ($p=0.1$) or ethnic ($p=0.4$) differences.

†Data not presented for other ethnic groups (Indian/Pakistani/Sri Lankan, $n=40$; Oceanic, $n=26$; Indigenous Australian, $n=10$; South American, $n=16$; African, $n=6$; and mixed/unknown, $n=152$).

‡Spherical equivalents: moderate hyperopia ($\geq+2.0D$); mild hyperopia ($+0.5$ – $+1.99D$); emmetropia (-0.49 – $+0.50D$); myopia ($\leq-0.50D$).

§Significantly greater than mild hyperopia group ($p<0.0001$).

learning difficulties, birth order, birth length, head circumference, birth weight, and gestational age.

Definitions

Anisometropia and aniso-astigmatism were defined as absolute interocular differences of spherical equivalent (SE, sphere + $\frac{1}{2}$ cylinder) and refractive astigmatism (RA), respectively. Prematurity was defined as gestational age <37 weeks, low birth weight <2500 g, and amblyopia as best visual acuity (VA) <0.3 logMAR units (Snellen $<20/40$), not explained by anatomical defects of the visual system, together with interocular VA difference ≥ 2 logMAR lines. Internal astigmatism was the vector difference between refractive and corneal astigmatism.²¹ Myopia was defined as SE $\leq-0.50D$, emmetropia as SE -0.49 to $+0.50D$, mild hyperopia as SE $+0.51$ to $+1.99D$, and moderate hyperopia as SE $\geq+2.00D$.

Statistical analysis

Analyses used Statistical Analysis System (v.9.1, Cary, NC, USA). Anisometropia/aniso-astigmatism prevalence was determined at ≥ 0.5 , ≥ 1.0 , ≥ 1.5 , and ≥ 2.0 dioptres (D). Prevalence variations by sex, ethnicity, and worse eye refraction were assessed using χ^2 test. Associations with

birth related, child related, and eye related parameters were explored using multiple logistic regression. Associations with amblyopia, strabismus, and refraction were based on the status of the worse eye. Associations with ocular biometry were also examined by comparing interocular differences in biometry between children with and without anisometropia/aniso-astigmatism (Kruskal-Wallis test).

RESULTS

Population characteristics

Of 1765 participants (78.9% of eligible), data on 1724 children (50.7% boys) were included in this report. There were no significant age ($p=0.8$), sex ($p=0.3$), or ethnic ($p=0.4$) differences for the 41 children excluded because of absence from school or missing data. Mean age (SD) was 6.7 (0.4) years (range 5.5–8.2 years). Mean SE was $+1.26D$ in right eyes (95% confidence interval (CI) $+1.23$ to $+1.31$), and $+1.31D$ (CI $+1.27$ to $+1.36$) in left eyes. The right/left eye SE correlation was 0.87 ($p<0.0001$); for RA, this was 0.67 ($p<0.0001$).

Prevalence

Table 1 shows prevalent anisometropia ($\geq 1.0D$). Anisometropia prevalence $\geq 0.5D$, $\geq 1.5D$, and $\geq 2.0D$ was

Table 2 Prevalence of aniso-astigmatism of at least 1.0D stratified by sex, ethnicity, and worse eye refraction, with 95% confidence intervals (CI)

	Number of children (%)	Prevalence (n = 17)	
		%	95% CI
All	1724 (100.0)	1.0	0.6 to 1.6
Girls	875 (50.8)	1.2	0.6 to 2.2*
Boys	849 (49.3)	0.8	0.4 to 1.7
Ethnicity†			
European white	1096 (63.6)	0.8	0.4 to 1.6*
East Asian	295 (17.1)	2.0	0.1 to 4.5
Worse eye refraction‡			
Moderate hyperopia	228 (13.2)	2.6	1.2 to 5.9§
Mild hyperopia	1384 (80.3)	0.7	0.3 to 1.3
Emmetropia	86 (5.0)	2.3	0.6 to 9.3
Myopia	26 (1.5)	0	–

*No significant sex ($p=0.4$) or ethnic differences ($p=0.09$).

†Data not presented for other ethnic groups (Indian/Pakistani/Sri Lankan, $n=40$; Oceanic, $n=26$; Indigenous Australian, $n=10$; South American, $n=16$; African, $n=6$; and mixed/unknown, $n=152$).

‡Spherical equivalents: moderate hyperopia ($\geq+2.0D$); mild hyperopia ($+0.5$ – $+1.99D$); emmetropia (-0.49 – $+0.50D$); myopia ($\leq-0.50D$).

§Significantly greater than mild hyperopia group ($p=0.008$).

Table 3 Associations with spherical equivalent (SE), anisometropia (n = 28), or aniso-astigmatism (n = 17) of at least 1.0D, presented as odds ratios (OR) and 95% confidence intervals (CI)

	Factor present		Factor absent		OR	95% CI	p Value
	No/total (%)	No/total (%)	No/total (%)	No/total (%)			
Anisometropia (SE)							
Amblyopia	15/31 (48.4)	13/1693 (0.8)	29.3	8.7 to 99.0*	<0.0001		
Strabismus	8/47 (17.0)	20/1676 (1.2)	0.8	0.2 to 3.4†	0.8		
Esotropia	3/26 (11.5)	20/1676 (1.2)	0.1	0.02 to 1.03‡	0.054		
Exotropia	5/20 (25.0)	20/1676 (1.2)	7.7	1.2 to 49.8†	0.03		
Low birth weight	4/92 (4.4)	18/1374 (1.3)	2.1	0.6 to 8.2‡	0.3		
Multiple births	4/47 (8.5)	22/1509 (1.5)	3.4	0.7 to 15.8§	0.1		
NICU admission	6/92 (6.5)	19/1410 (1.4)	3.6	1.1 to 12.6§	0.04		
Aniso-astigmatism							
Amblyopia	3/31 (9.7)	14/1693 (0.8)	8.2	1.4 to 46.7¶	0.02		
Strabismus**	2/47 (4.3)	15/1676 (0.9)	1.2	0.2 to 9.7††	0.8		
NICU admission	3/92 (3.3)	11/1410 (0.8)	4.6	1.2 to 17.2‡‡	0.02		
Maternal age >35 years	7/343 (2.0)	6/1196 (0.5)	4.0	1.3 to 11.9§§	0.03		
Paternal age >35 years	9/582 (1.5)	4/907 (0.4)	2.1	0.5 to 8.5¶¶	0.1		

*Adjusted for worse eye refraction, multiple birth and strabismus.

†Adjusted for worse eye refraction, multiple birth and amblyopia.

‡Adjusted for multiple births.

§Adjusted for low birth weight (<2500 g).

¶Adjusted for worse eye refraction, NICU, and maternal age.

**Number of esotropic/exotropic children were too small for separate analyses.

††Adjusted for worse eye refraction, NICU, maternal age, and amblyopia.

‡‡Adjusted for maternal age.

§§Adjusted for admission to a neonatal intensive care unit (NICU).

¶¶Adjusted for NICU and maternal age.

n = number of children with anisometropia (SE) or aniso-astigmatism.

Total sample = 1724.

6.2% (CI 5.1% to 7.5%), 0.9% (CI 0.5% to 1.4%), and 0.5% (CI 0.5% to 1.0%), respectively. Mean anisometropia was 0.21D (SD 0.41D). Anisometropia did not vary by age ($p > 0.2$), sex ($p > 0.06$), or ethnicity ($p > 0.1$). The prevalence difference between European white and east Asian children remained non-significant when analyses were performed for anisometropia at least 0.75D (2.7% v 3.4%, $p = 0.5$). Anisometropia (≥ 1.0 D) was significantly more prevalent in myopic and moderately than mildly hyperopic children. Among 28 children with anisometropia (≥ 1.0 D), two (7%) had bilateral myopia, one (4%) had unilateral myopia, one (4%) had mixed myopia/moderate hyperopia, two (7%) were emmetropic in one eye and mildly hyperopic in the other, 12 (43%) had unilateral moderate hyperopia, and 10 (36%) had bilateral moderate hyperopia.

Table 2 shows prevalent aniso-astigmatism (≥ 1.0 D). Prevalence of aniso-astigmatism ≥ 0.5 D, ≥ 1.5 D, and ≥ 2.0 D was 9.8% (CI 8.4% to 11.4%), 0.3% (CI 0.1% to 0.7%), and 0.2% (CI 0.06% to 0.5%), respectively. Mean aniso-astigmatism was 0.20D (SD 0.24D). Aniso-astigmatism did not vary by age ($p > 0.5$), sex ($p > 0.4$), or ethnicity ($p = 0.09$). The prevalence difference between European white and east Asian children was significant when analyses were performed for aniso-astigmatism at least 0.75D (4.4% v 1.8%, $p = 0.03$). Aniso-astigmatism was more prevalent in moderately than mildly hyperopic children. Among 17 children with aniso-astigmatism (≥ 1.0 D), two (12%) were bilaterally emmetropic, one (6%) was emmetropic in one eye and mildly hyperopic in the other, eight (47%) had bilateral mild hyperopia, two (12%) had unilateral moderate hyperopia, and four (24%) had bilateral moderate hyperopia. There were no cases of myopia in this group.

Associations

Of variables significantly associated with anisometropia (≥ 1.0 D) in unadjusted analyses, low birth weight and multiple birth became non-significant after multivariable adjustment (table 3). Multiple birth remained significant after adjusting for amblyopia and strabismus, but not after

also adjusting for low birth weight. Strabismus of all types was a significant predictor after adjusting for worse eye refraction and either multiple birth or NICU admission, but not after further adjusting for amblyopia or low birth weight. Prematurity was associated with anisometropia ≥ 0.5 D, $p = 0.036$, but this association was marginally non-significant after adjusting for age, sex, ethnicity, and worse eye refraction (OR 2.0, CI 0.99 to 3.9, $p = 0.055$).

Of factors significantly associated with aniso-astigmatism (≥ 1.0 D) in unadjusted analyses, paternal age >35 years and strabismus became non-significant after multivariable adjustment. Breast feeding had a significant protective association ($p = 0.02$) with aniso-astigmatism ≥ 0.5 D, OR 0.6 (CI 0.4 to 0.9), adjusted for age, sex, ethnicity, and worse eye refraction. This was significant ($p = 0.02$) in children not admitted to NICU or premature and with normal birth weight, OR 0.5 (CI 0.3 to 0.9). It was not significant, however, in children admitted to NICU ($p = 0.09$). A significant association (≥ 0.5 D) was also found for multiple births (OR 2.4, CI 1.2 to 5.1), adjusting for age, sex, ethnicity, and worse eye refraction.

Biometry

Anisometropic children had significantly greater interocular differences in AL and ACD, but not average corneal power, than non-anisometropic children (table 4). Children with aniso-astigmatism had significantly greater interocular corneal but not internal astigmatic differences than non-aniso-astigmatic children.

DISCUSSION

Prevalence

This population of predominantly 6 year old children had a low prevalence of anisometropia (1.6%) and aniso-astigmatism (1.0%), which did not vary by age, sex and ethnicity, but was greater at higher levels of ametropia.

Anisometropia and aniso-astigmatism prevalence could vary between studies because of different definitions, study methods, and population characteristics. Ideally, these

Table 4 Mean (SD) of interocular differences in ocular biometry between children with and without anisometropia or aniso-astigmatism of at least 1.0D

Biometric component	Children with condition	Children without condition
	Mean difference (SD)	Mean difference (SD)
Anisometropia (SE)	n = 28	n = 1696
Average corneal power (D)	0.28 (0.20)	0.22 (0.19)
Anterior chamber depth (mm)	0.10 (0.06)*	0.05 (0.04)
Axial length (mm)	0.72 (0.86)†	0.09 (0.08)
Aniso-astigmatism	n = 17	n = 1707
Corneal astigmatism (D)	0.87 (0.80)†	0.23 (0.20)
Internal astigmatism (D)	0.33 (0.25)	0.25 (0.21)

SE, spherical equivalent; mm, millimetres.

*Significant difference between anisometropic and non-anisometropic groups, $p < 0.001$.

†Significant difference between anisometropic and non-anisometropic groups, and between aniso-astigmatic and non-aniso-astigmatic groups, both $p < 0.0001$.

should have clinically meaningful definitions, such as recommendations of the American Association for Pediatric Ophthalmology and Strabismus.²² We used slightly lower cut offs to permit meaningful statistical examination of previously largely unexplored associations.

Previous studies reported anisometropia rates between 0% and 5%.^{4 10 11 13 18} Two large studies reported prevalences of 4.7% ($\geq 2.0D$)¹³ and 1.5%.⁴ However, children in the former study had retinoscopy¹³ while the refraction method in the second study was unclear.⁴ Studies that used similar methods and definitions reported prevalences of 3.4%¹⁰ to 3.8% (Singapore),¹⁸ 1.5% (urban Xiamen, China),¹⁰ 4.8% (rural Xiamen, China),¹⁰ and 1.4% (rural Japan).¹¹ The association of anisometropia with increasing ametropia is consistent with previous studies.^{15 16 23} Differences in the distributions of ametropia and anisometropia prevalence at each level of ametropia result in different overall anisometropia prevalences between different populations. For example, anisometropia prevalence among myopic, emmetropic, and hyperopic ($SE > +0.5D$) Singaporean children were 8.1%, 1.4%, and 0.6%, respectively.¹⁸ The overall anisometropia prevalence was contributed to almost equally by the similar prevalences of myopia (36%), emmetropia (30%), and hyperopia (34%) in their sample. In contrast, our overall low prevalence (1.6%) was driven primarily by a low prevalence (0.1%) among the 80.3% of children with mild hyperopia. It is interesting that anisometropia prevalence for each ametropia group was different between these two populations. Other influential factors contributing to this difference need to be considered.

Associations

Multivariate analyses of associations with anisometropia and aniso-astigmatism were limited by the small number of children with these conditions. Statistically significant associations were found both with NICU admission and amblyopia. Additionally, anisometropia and aniso-astigmatism were associated with exotropia and maternal age > 35 years, respectively. However, the confidence intervals for amblyopia and exotropia were quite wide, so conclusions about the magnitude of these effects should be made with this in mind. We did not find a statistically significant association with either low birth weight or prematurity, possibly because of the relatively low prevalence of very premature children (0.7% < 32 weeks). Previous studies have inconsistently reported an anisometropia association with low birth weight and retinopathy prematurity,^{4 6} possibly because these children continue to emmetropise with age, with a consequent reduction in anisometropia severity.⁶

Precise reasons for the association found with NICU admission is not known. It could be mediated by higher prevalence of subtle signs of retinopathy of prematurity, very

low birth weight, or extreme prematurity among such children.

Although we found strong associations between interocular refractive differences and amblyopia, the temporal relation of these associations cannot be determined from our cross sectional data. Anisometropia is known to cause amblyopia,^{2 24} and children in this study may have developed amblyopia after the onset of anisometropia. Although some previous studies suggest that amblyopia may lead to the development of anisometropia,^{25 26} our cross sectional data cannot confirm this.

Although children of older mothers were more likely to be premature, and to have lower birth weight and congenital abnormalities,²⁷ the association of older maternal age and aniso-astigmatism could be mediated via different mechanisms as aniso-astigmatism was not associated with either low birth weight or prematurity.

We found no significant anisometropia associations with smoking or breast feeding, though breast feeding was significantly associated with lower aniso-astigmatism ($\geq 0.50D$). This builds on recent findings indicating a protective effect of breast feeding on myopia.⁹

Biometry

The association of anisometropia with increased difference in AL but not corneal power between eyes is similar to a study in children with a high (36%) myopia prevalence ($SE < -0.50D$).¹⁸ We have found that it is also associated with an interocular difference in ACD. We also found that aniso-astigmatism resulted from an interocular difference in corneal but not internal astigmatism. These findings have several implications. Firstly, as our study population is largely hyperopic, hyperopia may be predominantly axial in origin. Secondly, changes in ACD are associated with changes in refractive errors. Thirdly, changes in RA are mainly corneal in origin.

In conclusion, we found relatively low prevalence rates for anisometropia and aniso-astigmatism, both of which were more prevalent with increasing ametropia. Amblyopia and NICU admission significantly increased the odds of both conditions. Exotropia and maternal age more than 35 years, respectively, were also associated with increased odds of anisometropia and aniso-astigmatism. Biometric associations included AL and ACD for anisometropia, and CA for aniso-astigmatism.

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Authors' affiliations

S C Huynh, J Ip, D Robaei, A Kifley, P Mitchell, Centre for Vision Research, Department of Ophthalmology and Westmead Millennium Institute, University of Sydney, Sydney, Australia
K A Rose, School of Applied Vision Sciences, Faculty of Health Sciences, University of Sydney, Sydney, Australia
X Y Wang, Vision Cooperative Research Centre, School of Optometry, University of New South Wales, Sydney, Australia

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