

The evolution of refractive status in Chinese infants during the first year of life and its affected factors

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Abstract

• **AIM:** To study the evolution of the refractive status and examine the affected factors in infants during the first year of life in a large sample size in China.

• **METHODS:** A total of 1258 babies (2516 eyes) aged 32wk gestational age to 1y participated in the study, including 766 premature and 492 full-term infants. First, each baby received an orthoptic examination, slit-lamp checking and fundus imaging. Patients with diseases which might affect refractive status were excluded from the cohort. The cycloplegia retinoscopy was performed. Their neonatal histories were reviewed. Each measurement contained the refractive status and calculation of the spherical equivalent (SE).

• **RESULTS:** Refractive state showed an average hyperopia of $+0.94 \pm 1.63$ D at early ages, followed by a trend toward more hyperopia. The refractive state reached the top ($+2.43 \pm 1.46$ D) at the age of one to two months. Then gliding till one year old when the refractive state reached $+0.59 \pm 1.41$ D. The prevalence of astigmatism was 42.17% in the study, being 2.82% myopic astigmatism and 39.35% hyperopic astigmatism. The 94.1% of hyperopic astigmatism was with-the-rule astigmatism and 71.83% of myopic astigmatism was with-the-rule astigmatism. Refractive state between boys and girls was different. The mean SE of boys was $+1.97 \pm 1.57$ D, while that of girls was $+1.79 \pm 1.46$ D, and the difference was significant.

• **CONCLUSION:** Before one year old, the change of refractive status is associated with checking age and sex. At the age

of one to two months, the degree of hyperopia reaches the top. Boys have more hyperopic degree than girls, and with-the-rule astigmatism is predominant. Excluding premature infants with advanced retinopathy of prematurity, premature and full-term children have same refraction status.

• **KEYWORDS:** refractive status; corrected age; infant, prematurity; spherical equivalent; cycloplegic retinoscopy
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INTRODUCTION

Refractive error is a major eye care problem throughout the world^[1-2] and ametropia is known to increase the risk of amblyopia and strabismus^[3]. In order to early intervene for refractive error, it is necessary to understand the starting point of refractive error at birth and the corresponding refractive status of different development stage. It is well-known that eye refraction changes with age, and young children are generally hyperopic^[4-11]. Compared with full-term infant, premature infants especially low birth weight premature tend to develop myopia in the future^[12-18]. However, subjects of most studies were started measurements after one to three years of age. There were only a few studies about refractive error especially before one year old^[10]. And most of them were in small samples. Because of the limitation of age and check condition, large samples size were few.

The aim of our study is to find the evolvement rule of refractive status at early development stage, by investigating the refractive status of premature infants and full-term infants in China during the first year of life with large samples. These data would provide essentially normative information for screening program.

SUBJECTS AND METHODS

Subjects This is a retrospective cohort and cross-sectional study. A total of 1258 children (2516 eyes) participated in this study. It comprised 766 premature infants (26-36wk of gestation, the mean gestation age was 32.23wk), and 492 full-term infants (37-44wk of gestation, the mean gestation age was 39.17wk) who were given an eye examination at Qilu Children's Hospital of Shandong University, from January 2014 to August 2016. For premature infants, most of them came to the hospital to perform retinopathy of

prematurity (ROP) screening, and the rest were for ophthalmic examination. The corrected gestation ages at the checked point were between 32wk and one year old. Informed consent was obtained from one or both parents before each infant was enrolled. The research was in agreement with the Declaration of Helsinki.

Variables and the Measurements

Common examination First, each baby received an orthoptic examination including cover and motility tests; and then the eye was examined with handheld slit lamp, cycloplegia retinoscopy, and fundus images were taken. Eyes with nystagmus, strabismus, single or double ptosis, advanced ROP with laser-treated or intravitreal injection, or any other retinal morbidity were excluded from the study. Eyes with spontaneously regressed ROP were retained in the study. Children whose parents had genetic eye diseases were also not considered.

Refractive examination Cycloplegia for retinoscopy was achieved with one or two drops 0.5% cyclopentolate hydrochloride and three to five drops 0.5% phenylephrine hydrochloride every 10min. Streak retinoscopy (66 Vision Technology, Suzhou, Jiangsu Province, China) was performed 30min afterward. All refractive measurements were performed by the same experienced senior optometrist. An allowance of 2.0 D was allowed for a working distance of half meter.

Data recording The original data comprised the date of examination, name, sex, gestational age (GA), birth weight (BW), corrected gestational age (CGA), now weight (NW), right or left eye, clinical diagnosis, sphere, cylinder and its axis. Refractive error was recorded in the form of spherical equivalent (SE)=sphere+1/2cylinder. Myopia was defined as SE less than or equal to -0.50 D, and hyperopia was defined as SE more than or equal to +0.50 D. Astigmatism was defined as cylindrical degree (CD) greater than or equal to ±0.50 D. In this study, corrected age equals to postnatal age minus the difference between term (40wk) and GA at birth. For instance, the CGA of an infant born at 28wk GA and tested at postnatal age 24wk was 12wk: 24-(40-28)=12. An infant born at 38wk GA and tested at postnatal age 6wk was 4wk: 6-(40-38)=4. We referred to “corrected gestational age” as “age” in this report unless special instructions.

Statistical Analysis In this study, sphere, cylinder and its axis for each measurement were recorded, and then calculated the SE for each measurement was calculated. SPSS 11.0 software was used for all statistical analysis. Statistical significance was defined as P value less than 0.05. Correlations between eye refraction and the different variables were analyzed with regression and Pearson correlation tests. Because of highly correlated with age and weight, the partial correlation analysis was performed on the relationship between SE and body weight. The correlation between double eyes was performed with paired samples t-test.

RESULTS

A total of 1258 babies (2516 eyes) participated in this study,

Table 1 Correlations and differences between SE and some factors

Factors	r	P
BBW	0.032	0.112
NBW	0.019	0.336
Right or left	0.001	0.970
CGA	0.107	0.000
Sex	-0.053	0.008

BBW: Birth body weight; NBW: Now body weight; CGA: Corrected gestation age. Correlation was significant at the 0.05 level (2-tailed).

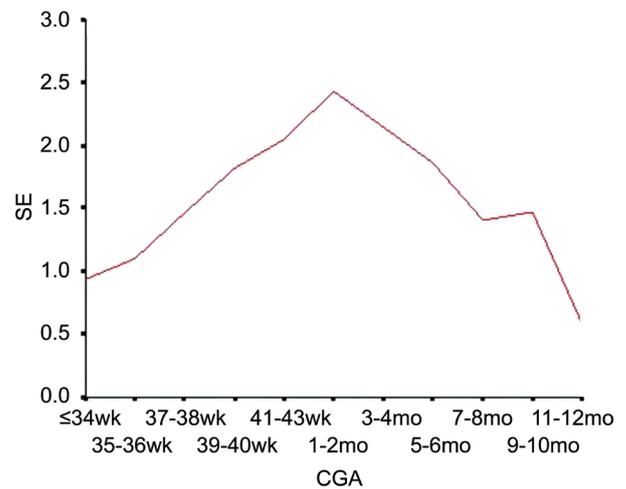


Figure 1 SE refraction in different CGA.

including 782 boys (62.2%) and 476 girls (37.8%), among them there were 766 premature infants (62.16%) and 492 full term infants (37.84%).

Comparison of Refraction with Some Factors With correlation and regression analysis, it was demonstrated that eye refraction was related with its CGA and sex, but not with its birth body weight (BBW), now body weight (NBW), right or left eye (Table 1). At the same checked age, there was no significance between SE and birth gestational age (BGA) (P>0.05). A high correlated coefficient was found between double eyes about SE (r=0.933) by paired samples t-test. The difference of refraction between double eyes is not significant (P=0.000) (Table 1).

Refraction and Age All samples were divided into eleven groups according to CGA. Refractive degree showed an average hyperopia of +0.94±1.63 D at the beginning of the study, followed by a trend toward more hyperopia. The refractive degree reached the top (+2.43±1.46 D) at the age of about one to two months. Then gradually decline, the refractive degree reached +0.59±1.41 D at the age of one year old (Table 2; Figure 1).

Refraction and Sex Refractive degree of different sex was different in this study. The mean SE of boys was +1.97±1.57 D, and girls was +1.79±1.46 D. Boys had more hyperopia degree than girls at different ages (Table 3; Figure 2).

Astigmatism A total of 2516 eyes were enrolled into the study. Among them 1061 eyes (42.17%) existed astigmatism, including 71 myopic astigmatism eyes (2.82%) and 990

Table 2 Mean SE refraction in different CGA

CGA	Eyes (n)	Mean SE	SD	Std. Error		95%CI for mean	Min	Max
				Lower bound	Upper bound			
≤34wk	26	+0.94	1.63	0.32	+0.28	+1.59	-4.75	+2.75
35-36wk	130	+1.10	1.47	0.13	+0.85	+1.36	-3.00	+4.00
37-38wk	386	+1.46	1.63	0.08	+1.31	+1.63	-3.75	+6.00
39-40wk	438	+1.81	1.46	0.07	+1.69	+1.96	-2.25	+6.38
41-43wk	392	+2.05	1.39	0.07	+1.90	+2.17	-2.00	+6.00
1-2mo	582	+2.43	1.46	0.06	+2.31	+2.55	-2.50	+8.00
3-4mo	270	+2.15	1.42	0.09	+1.98	+2.32	-0.75	+6.25
5-6mo	154	+1.87	1.58	0.13	+1.61	+2.12	-0.75	+9.50
7-8mo	74	+1.41	1.58	0.15	+1.12	+1.70	-0.50	+6.38
9-10mo	42	+1.48	1.25	0.22	+1.04	+1.92	-1.75	+4.50
11-12mo	22	+0.59	1.41	0.20	+0.17	+1.02	-1.13	+2.13
Total	2516	+1.90	0.96	0.03	+1.85	+1.97	-4.75	+9.50

CGA: Corrected gestation age.

Table 3 Mean SE refraction of boys and girls

CGA	Male			Female		
	Eyes (n)	Mean SE	SD	Eyes (n)	Mean SE	SD
≤34wk	20	1.07	1.73	6	0.50	1.25
35-36wk	84	1.00	1.55	46	1.28	1.32
37-38wk	232	1.63	1.67	154	1.22	1.55
39-40wk	258	2.00	1.41	180	1.55	1.50
41-43wk	218	2.02	1.41	174	2.07	1.36
1-2mo	380	2.55	1.50	202	2.21	1.37
3-4mo	172	2.09	1.39	98	2.24	1.46
5-6mo	108	1.90	1.77	46	1.78	1.05
7-8mo	48	1.24	1.30	26	1.72	1.13
9-10mo	28	1.38	1.59	14	1.67	0.95
11-12mo	16	0.77	0.94	6	0.11	0.90
Total	1564	1.97	1.57	952	1.79	1.46

CGA: Corrected gestation age.

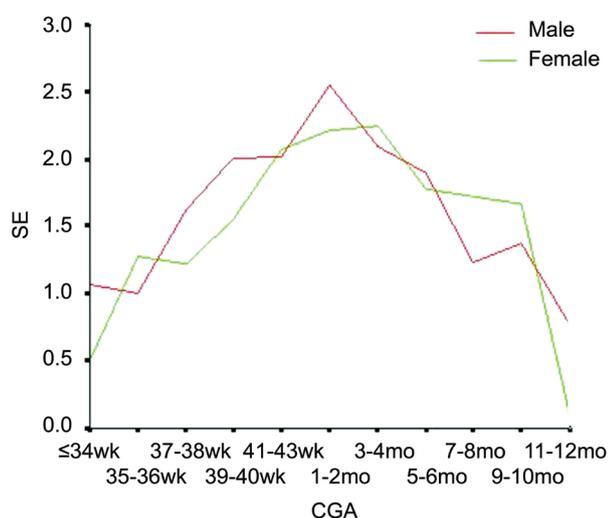


Figure 2 SE refraction of boys and girls.

hyperopic astigmatism eyes (39.35%). The minimum myopic cylindrical power was -3.50 D, and the maximum hyperopic cylindrical power was +4.00 D. The 94.37% myopic and 93.94% hyperopic astigmatism degree were below 2.00 D (Table 4).

Figures 3, 4 showed the magnitude and axis of cylindrical power. The 94.1% of hyperopic astigmatism was with-the-rule astigmatism and 71.83% of myopic astigmatism was with-the-rule astigmatism.

DISCUSSION

Mean Spherical Equivalent Refraction Our study provided a detailed analysis with several unique findings about the refractive status during the first year of infancy. The changes of eye refraction tend to more hyperopic with the age, then hyperopic degree gradually declined, until emmetropia or myopia. This rule is consistent with those former reports^[3-5,17,19-20]. The crystalline lens of premature is near the cornea and is relatively spherical in shape, which leads to shallower anterior chamber and more highly curved cornea compared with eyes of full-term infant^[5]. The lens change rapidly during the last trimester with flattening and moving away from the cornea, which results in thinner lens thickness, shallower anterior chamber and smaller corneal curvature. Thus, we believe that there is a large refractive shift from myopia to hyperopia before the time of full-term birth. Cook *et al*^[5] referred that the components of refractive state showed linear patterns of growth up until 44wk postmenstrual age. In our younger patients, the refractive was +0.94 D at the corrected gestational age of 34wk, then hyperopic degree increased gradually. At the age of 1-2mo, the refractive reached the top value (+2.43±1.46 D) and then declined. At the age of one year, the refractive reached to +0.59 D. Cook *et al*^[5] reported that refractive state showed an average myopia of -2.00 D at the age of 32wk. These results verified that refractive developed from myopia in embryonic period, then followed by a trend toward hypermetropia.

Table 4 Mean cylindrical power of premature and full-term infants

Parameters	Astigmatism	Eyes (n)	Prevalence (%)	Mean (D)	SD	Max/Min	≤±2.00 D (eyes)	≤±1.00 D (eyes)
Premature	Myopic	38	2.42	-1.14	0.59	-3.00	36 (94.74)	24 (63.16)
	Hyperopic	483	31.53	+0.99	0.56	+3.25	461 (95.45)	351 (72.67)
Full-term	Myopic	33	3.25	-1.23	0.65	-3.5	31 (93.94)	17 (51.52)
	Hyperopic	507	51.52	+1.14	0.63	+4.0	469 (92.50)	318 (62.70)
Total	Myopic	71	2.82	-1.19	0.61	-3.50	67 (94.37)	41 (57.75)
	Hyperopic	990	39.35	+1.07	0.60	+4.00	930 (93.94)	669 (67.58)

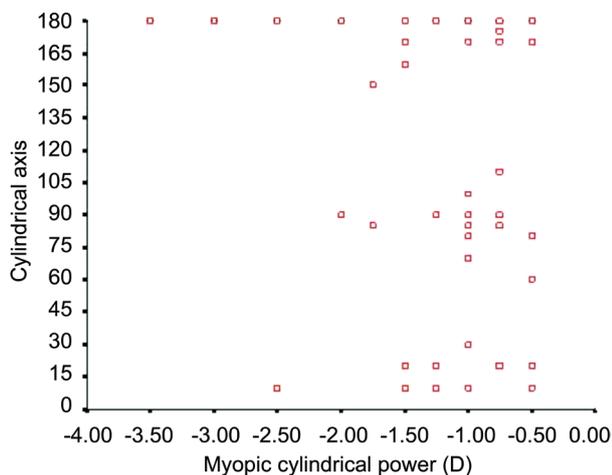


Figure 3 Myopic cylindrical power and axis.

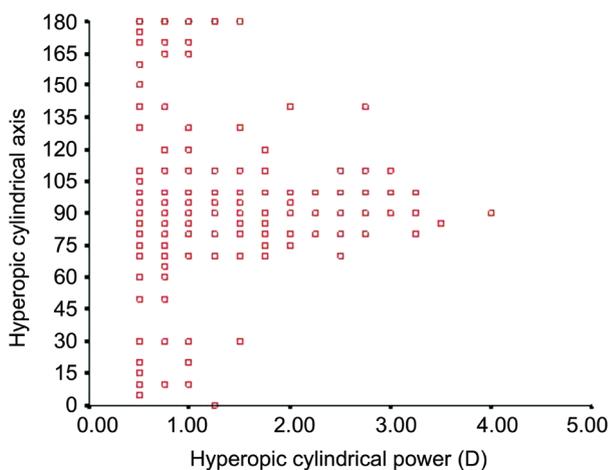


Figure 4 Hyperopic astigmatic degree and axis.

Ton *et al*^[4] referred that the mean refractive of infants was +1.24 D in infants aged 1mo or less and reached to +2.50 D at the age of 4-6mo. Gunay *et al*^[6] and Mutti *et al*^[7] showed a mean refractive error of about +2.2 D from the first to the fourth month of age then declined. Wood *et al*^[11] showed a mean spherical equivalent error of +1.44 D for 58 infants at 2wk of age, which increased to +2.84 D at 12wk of age. Our result was in agreement with them. Chen *et al*^[3] found the mean cycloplegic spherical equivalent was highly hyperopic (OD, +3.47±2.43 D; OS, +3.64±2.43 D) for full-term Chinese neonates who were between 1d and 6d of age, whose hypermetropia was about 1 D greater than that of our results.

Astigmatism The prevalence of astigmatism was 42.17% in this study, including 2.82% myopic astigmatism and 39.35%

hyperopic astigmatism. It was consistent with previous reports^[13]. It was shown that the magnitude and proportion of astigmatism and myopia of premature were greater than that of full-term infants, especially with advanced ROP^[14-15,19]. Astigmatism is mainly influenced by corneal curve, and premature with advanced ROP has highly curved corneas^[10]. Lu *et al*^[14] referred that patients with aggressive posterior retinopathy of premature (APROP) who underwent laser treatment tend to have more severe astigmatism, but no significant differences between APROP and the non-APROP. In this study, premature had 2.42% myopic astigmatism and 31.53% hyperopic astigmatism, the mean degrees were -1.14 D and +0.99 D respectively. While full-term had 3.25% myopic astigmatism and 51.52% hyperopic astigmatism, the mean degrees were -1.23 D and +1.14 D. The two distributions between premature and full-term were significantly different ($P=0.000$). One reason was that we excluded those premature with advanced ROP which had more risk to develop astigmatism. Another possible reason was that some full-term infants felt fear and crying when checking and eye speculum had to be used to open the eyelids, which might increase the astigmatism degree.

Refraction and Other Factors Our study showed that refraction had a positive linear correlation with age. Many studies^[4-11] referred that eye refraction was correlated with age at the time of examination, but not with birth weight or gestational age. However, low birth weight and ROP have long been known to be implicated in the development of myopia, astigmatism, and anisometropia. Children with laser treatment for ROP tend to have higher risk^[10,13-16,18,20-21]. However, there were no significant differences in the refractive status in patients with regressed ROP and in preterm infants without ROP^[14]. In this study premature infants with advanced ROP or APROP were excluded, but regressed ROP were reserved.

Our study found that eye refraction was connected with age at the time of examination and sex. Boys had higher hyperopic degree than girls. The difference between boys and girls was significant ($F=8.215$, $P=0.004$). This result was different from most previous research results^[4-11,22-24]. Kleinstein *et al*^[25] referred that the prevalence of myopia in boys was higher than that in girls. In China some research showed that myopia was associated with female^[26-27]. Our result showed that male had more hyperopia than that of female, which implied that females

had more feasibility to develop myopia. But the evidence was not sufficient. Further long follow-up study will be needed to confirm.

After adjusting the checking age, eye refractions had no relation with birth gestational age, birth body weight and now body weight. Excluding premature infants with APROP or advanced ROP, premature and full-term children had same refraction status and no significant differences between two distributions ($P>0.05$).

As the samples size of different age groups in the study was not matched, especially at the age from 7mo to one year old, this might lead to inaccuracy of the results. Our results only showed the refractive status of infants before one year, and it could not represented the whole refractive evolution of children. The importance of long-term follow-up should be emphasized.

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