

Accepted Manuscript

Myopia Progression in Low Birth Weight Infants: A Narrative Review

Running title: Myopia Progression

Amir Ahmadzadeh-Amiri¹, Majid reza Sheikhezade², and Ahmad Ahmadzadeh-Amiri^{2*}

¹Department of Pediatric, Bahrami-Hospital, Tehran University of Medical Sciences, Tehran, IR
Iran

^{2,2*}Department of Ophthalmology, Clinical Research Development Unit of Bu-Ali Sina
Hospital, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, IR Iran,

2*- Corresponding author: Ahmad Ahmadzadeh Amiri, MD., Assistant Professor of
Ophthalmology

Postal Address: Department of Ophthalmology, Mazandaran University of Medical Sciences,
Bu-Ali Sina Hospital, Pashadan Boulevard, Sari, IR Iran

Tel& Fax: +98 11 33344506

E-mail: ahmadzdh@yahoo.com

ORCID IDs of all authors (If any):

Amir Ahmadzadeh Amiri: 0000-0001-5560-3472

Majid reza Sheikhezade: 0000-0002-1105-7294

Ahmad Ahmadzadeh Amiri: 0000-0002-2700-5480

To appear in: Journal of Pediatrics Review

Received: 2019/06/11

Revised: 2019/09/01

Accepted date: 2019/09/14

This is a “Just Accepted” manuscript, which has been examined by the peer review process and has been accepted for publication. A “Just Accepted” manuscript is published online shortly after its acceptance, which is prior to technical editing and formatting and author proofing. Journal of Pediatrics Review provides “Just Accepted” as an optional and free service which allows authors to make their results available to the research community as soon as possible after acceptance. After a manuscript has been technically edited and formatted, it will be removed from the “Just Accepted” web site and published as a published article. Please note that technical editing may introduce minor changes to the manuscript text and/or graphics which may affect the content, and all legal disclaimers that apply to the journal pertain.

Please cite this article as:

Amiri Ahmadzadeh Amiri¹, Majid reza Sheikhrezaee², and Ahmad Ahmadzadeh Amiri^{3*} Myopia Progression in Low Birth Weight Infants: A Narrative Review. J. Pediatr. Rev. Forthcoming 2020 April 30.

Abstract

Context: Low birth weight infant is prone to an altered ocular development in childhood, including refractive errors of the eye. Myopia (short-sightedness) is the most common refractive error disease of the eye that causes reduced vision globally.

Evidence Acquisition: A PubMed literature search was conducted using the following search terms; low birth weight infant, myopia, prematurity, and refractive error.

Results: Commonly, the underlying cause of myopia is excessive growth of the eye which is under the influence of early life impression on human growth. Children with low birth weight have significantly shallower anterior chamber depth and greater lens thickness. At the ages of 10–12 years, preterm children have an increased likelihood of all refractive error statement. However, in low birth weight children, a 1 diopter of myopic change has occurred over the first decade of life.

Conclusion: The progression of myopia is higher in children with low birth weight, suggesting that prematurity and low birth weight may simultaneously affect the development of optical components, leading to myopia.

Keywords: Myopia, Refractive Error, Low Birth Weight, Premature infant

1. Context

Introduction of the intensive care units into newborn nurseries has led to a significant increase in the survival rate of preterm infants, and there has been a notable worry that it might also have given rise to an increased incidence of severe neurosensory disabilities (1, 2).

Several studies have shown that the occurrence of myopia in children born prematurely (gestational age [GA] ≤ 37 weeks) is negatively correlated with GA and birth weight (3-6).

Refractive errors include myopia (spherical equivalent ≥ -0.75 diopters [D] extreme), high myopia (spherical equivalent ≥ -6.00 D extreme), moderate or mild myopia (-0.75 to -5.99 D), emmetropia (no refractive error, -0.74 to $+0.99$ D), hypermetropia (long-sightedness $+1.0$ D extreme), and astigmatism (≥ 1 D cylinder and anisometropia (≥ 1 D difference in the mean spherical equivalent refraction between the two eyes). (7-9)

Relative mild to moderate myopia currently affects 25% of populations in western countries, at least 5% in Africa, and up to 80% in eastern Asia. In contrast to this, high myopia (very severe and pathologic) affects less than 3% of the worldwide populations. (10)

Researchers emphasize the association between myopia and low birth weight for gestational age, gender, greater maternal age, maternal smoking, and higher paternal occupational social class confidently. There was some evidence that even a short period of breastfeeding decrease myopia progression (10).

Low birth weight (LBW) infants (birth weight less than 2,500 grams) are exposed to three risk factors that affect the visual outcome; the presence of retinopathy of prematurity (ROP), neurological comorbidities and preterm birth itself. However, little survey exists about the myopic progression in growing children who were born with low birth weight. In this study, we only present and discuss the findings of recent investigations in which the impact of LBW on myopia development during childhood and changes over a wide range of age were assessed.

2. Evidence Acquisition

A PubMed literature search limited to the English language from 1997 to 2019 was conducted using the following search terms; low birth weight infant, myopia, prematurity, and refractive error. Herein, qualitative results taken out from research studies are provided and discussed.

The articles were then reviewed to exclude those refractive errors related primarily to normal birth weight, adult cases without any childbirth history and studies in nonrefractive low vision subjects as these were not the scope of this review. For the aim of this review, case-control, randomized controlled trials, cohort studies, evidence from meta-analyses, and systematic reviews were considered. Case reports or case series were included only if there were defined as evidence by more than two articles to unify uncommon findings as an index of future research. We excluded articles considering skillful viewpoints and letters to the editor. A total of 615 potentially relevant records were identified. Following the exclusion of 308 reports, 307 full-text papers were retrieved for gloss inspection. A total of 31 articles matched the eligibility criteria.

3. Results

3.1. Risk factors assessment

Patients with LBW often encounter visual impairment. Refractive status is related to multiple optical components, and corneal curvature, anterior chamber depth, lens thickness, vitreous thickness, and axial length.

Ouyang et al. showed the far greatest predictors of myopic development are indices of immaturity; short GA and LBW, of which the prematurity and low birth-weight are more important than the others. They conclude that the birth-weight held a negative relationship with corneal astigmatism, astigmatism, and corneal refractive power, while being positively associated with the corneal radius of curvature, vitreous thickness and ocular axial length (11).

Regarding the above-mentioned conclusion, Chen et al. found that the myopia cases born prematurely had significantly shallower anterior chamber depth and greater lens thickness (12). Moreover, O'Connor et al. showed that the refractive state is relatively constant over the first decade of life with a shift towards myopia of one diopter in low birth weight children (13). Particularly more, in premature children both with and without ROP, elevated corneal curvature, reduced anterior chamber depth, increased lens thickness, and decreased axial eye length have been observed (14, 15).

Additionally, Zhu et al. revealed in a case-control study that the incidence of myopia was significantly different in preterm children with ROP, preterm children without ROP, and in full-term children aged 6 years old (14.29%, 6.73%, and 2.22% respectively), which were higher than that reported in children aged 3 to 5 years (15, 16).

However, the refractive outcome of preterm birth is not confined to only this condition and an increase all forms of refractive errors have also been reported in other studies. In this regard, Fledelius reported that some cases of early myopia, also called myopia of prematurity later showed a reduction in the degree of myopia over 1-2 years (17). While Quinn et al demonstrated that changes in refractive error distribution occur primarily between 3 months and 1 year and include a decrease in the proportion of eyes with hyperopia and an increase in the proportion with high degrees of myopia (18).

In fact, in a 3.5-year ophthalmological long term follow up study of 248 preterm infants, Holmström et al. compared subjects with the refractive errors risk. Holmström highlighted how prematurity such as Cryo-treated infants was more significantly associated with the onset of myopia rather than infants born at term (19). Moreover, a cross-sectional study in 10-year-old prematurely born Swedish children revealed that these children had a higher prevalence of hypermetropia of more than 3 D, or myopia of -1 D or less, astigmatism of 1 D or more, and anisometropia of 1 D or more than those born at term (20).

In a recent cohort study of very LBW infants at 27-29 years in New Zealand, identified a history of untreated ROP was associated with a higher likelihood of high myopia(>5D) progression (21).

A Randomized controlled clinical trial study demonstrated that nearly 70% of the eyes that had high-risk pre-threshold ROP were likely to be myopic during childhood and that the proportion with high myopia has increased between the ages of 6 months and 3 years old (22). Another report of this Early Treatment for Retinopathy of Prematurity trial group also showed that approximately two-thirds of eyes that had high-risk pre threshold ROP during the neonatal period are likely to be myopic into the 6 years of life. They also confirmed that conventional management in comparison with the earlier treatment of eyes with high-risk pre-threshold ROP did not impress more refractive errors' development (23).

The Apgar score is broadly used as an index of the health status of neonates immediately at birth, can be used as a predicting mortality factor in extremely low birth weight infants (24). As comparing subjects with the term infants; premature neonates are more susceptible to birth problems, highlighted the Pan et al. finding that showed the influence of the low Apgar score and the risk for the child of developing myopia (25).

According to the National Vital Statistics Report, the risk of preterm birth was more than 12 times higher in twins than singletons (26). Thus, given the results in Avnon et al. study, comparison of refraction between preterm infants from singletons and multiples pregnancy disclosed no differences at the age of 6 months old, while at the ages of 8-12 years old, multiples had significantly more myopic refractive errors (27).

Hence, we should consider myopia as a more complex pattern, where prematurity and low birth weight is crucial to the development of the disease. Table 1 demonstrates earlier studies implicated refractive states with and without ROP according to the age of examination to the progression of myopia. The studies varied from infancy to adult age group.

3.2.Impact on the ocular structure and refractive status

More immature preterm newborns are more likely to develop adverse visual effects other than those imputable to ROP. The shortened gestational periods up to 40%, pointed out that other features of the visual system, e. g. cerebral white matter is vulnerable to disturbances (32).

Emmetropization is the action in refractive development of eye whereby the ocular growth is in a harmonized manner to make an eye without refractive error (33). This precise visually set process is threatened in a preterm baby because of the following reasons: first, the effect of being born with a LBW and second, as a sequel of ROP.

The shortened intrauterine period in preterm birth deprives the fetus of a protective environment that normally promotes visual growth and development. Fledelius illustrated that the eyes of preterm babies even without ROP do not grow naturally (34).

Studies have shown that the anterior segment of the eye which plays a fundamental role in focusing the light onto the retina, was different between term and preterm infants: corneas of preterm children are more curved, and the lens is thicker, both of which increase the focusing power of the eye, leading to low degree myopia. This is not due to ROP and is alluded to as myopia of prematurity (34, 35).

Table 1. Characteristics of included studies of low birth weight myopic progression				
BW/GA	ROP prevalence	Age	Refractive errors	Study
<27 weeks 348-1315 g	73.7% (20.4% treated)	30 months	25.6%—all myopia of 6 D or more was found in 2.5%	EXPRESS 2013(28) Sweden study
<1251 g	All reached threshold (82.5% bilateral)	3.5 years	Moderate myopia (≥ 2 D to <6 D): ► Treated eyes 20.5% ► Untreated eyes 15.5% High myopia (≥ 6 D): ► Treated eyes 37.7% ► Untreated eyes 27.2%	CRYO-ROP Study 2000(29)
<1251 g	High-risk prethreshold	6 years	Myopia $\geq 65\%$ in all treated eyes High myopia $\geq 35\%$ in all treated eyes	ETROP 2000-2002(30)
<1501 g	39%	10 years	Moderate myopia 3.8% Moderate hypermetropia 4.2% Astigmatism 21%	Larsson and Holmström 2003(20)
<1701 g	50%	10–12 years	Mild myopia 15.2% Moderate myopia 3.8% Moderate hypermetropia 6.6%	O'Connor et al 2005(13)
<1500 g	21%	27–29 years	No differences in myopia (>2 D) between the groups but high myopia (>5 D) was confined to those with ROP.	the NZ 1986 VLBW follow-up study 2017(21)
<2500 g	23%	3-4 years	Myopia was 5.08% of ROP group, but not in control group. Hyperopia and astigmatism were the highest in control group, followed by ROP group	Ouyang et al. 2009 to 2011 (11)
low: <2500g; normal: between 2500 and 4000 g; and high: >4000 g	Data not available	35 - 74 years	Comparison between three groups in a cohort study showed Individuals with low BW are more likely to have lower visual acuity and a higher myopic refractive error in adulthood.	Fieß A et al. Gutenberg Health Study in Germany 2019 (31)

BW, birth weight; D, diopter; GA, gestational age; ROP, retinopathy of prematurity.

4. Conclusions

These reviews demonstrate an association between LBW and altered ocular geometry in the long term, and suggest that birth weight and the associated factors are important in refractive errors' evolution. Severe ROP has increased the risk of myopia. A mild degree of ROP does not contribute additionally, other than prematurity, to this deduction. Early treatment of ROP may improve retinal pathology but could not influence refractive error development, although it is clear that the incidence of myopia varied when the zone of ROP or plus disease was noted. In general, premature newborns, with or without ROP, are susceptible to myopia. These findings support the importance of repeated assessment of refractive error over the first decade of life in infants who had LBW.

Acknowledgements

The authors would like to offer their thanks to Clinical Research Development Unit of Bu-Ali Sina Hospital for cooperation in search strategies.

Ethical Considerations

This research had no ethical consideration.

Funding

There is no specific grant to be received doing this research.

Author's contributions

All three authors contribute to literature searches, compiled and approved the final manuscript.

Conflicts of interest

The authors have no financial or personal relations that could state a conflict of interest.

References

1. Picciolini O, Squarza C, Fontana C, Gianni ML, Cortinovis I, Gangi S, et al. Neurodevelopmental outcome of extremely low birth weight infants at 24 months corrected age: a comparison between Griffiths and Bayley Scales. *BMC Pediatr* 2015; 15:139.
2. Raju TNK, Buist AS, Blaisdell CJ, Moxey-Mims M, Saigal S. Adults born preterm: a review of general health and system-specific outcomes. *Acta Pædiatrica* 2017; 106:1409–1437
3. Fledelius HC. Ophthalmic changes from age of 10 to 18 years. A longitudinal study of sequels to low birth weight. I. Refraction. *Acta Ophthalmol (Copenh)* 1980; 58(6):889-98.
4. O'Connor AR, Stephenson TJ, Johnson A, Tobin MJ, Moseley MJ, Ratib S, et al. Long term ophthalmic outcome of low birth weight children with and without retinopathy of prematurity. *Pediatrics* 2002; 109:12–18.
5. Stephenson T, Wright S, O'Connor A, Fielder A, Johnson A, Ratib S, et al. Children born weighing less than 1701 g: visual and cognitive outcomes at 11-14 years. *Arch Dis Child Fetal Neonatal Ed.* 2007; 92(4):F265-70.
6. Rodríguez-Abrego G, Sotelo-Dueñas HM. [Myopia prevalence among school-age children in a suburban population]. *Rev Med Inst Mex Seguro Soc.* 2009;47(1):39-44.
7. Dandona R, Dandona L. Refractive error blindness. *Bull World Health Organ* 2001; 79:237–43.
8. Deng L, Gwiazda JE. Anisometropia in Children from Infancy to 15 Years. *Investigative Ophthalmology & Visual Science* 2012; 53(7): 3782-3787
9. Kempen JH, Mitchell P, Lee KE, Tielsch JM, Broman AT, Taylor HR, Ikram MK, Congdon NG, O'Colmain BJ; Eye Diseases Prevalence Research Group. Prevalence of refractive errors among adults in the United States, Western Europe, and Australia. *Arch Ophthalmol* 2004; 122:495–505.
10. Rahi JS, Cumberland PM, Peckham CS. Myopia over the Life course: Prevalence and Early Life Influences in the 1958 British Birth Cohort. *Ophthalmology* 2011; 118:797–804
11. Ouyang LJ, Yin ZQ, Ke N, Chen XK, Liu Q, Fang J, et al. Refractive status and optical components of premature babies with or without retinopathy of prematurity at 3-4 years old. *Int J Clin Exp Med.* 2015; 8(7):11854-61.
12. Chen TC, Tsai TH, Shih YF, Yeh PT, Yang CH, Hu FC, et al. Long-term evaluation of refractive status and optical components in eyes of children born prematurely. *Invest Ophthalmol Vis Sci* 2010; 51:6140–8.
13. O'Connor AR, Stephenson TJ, Johnson A, Tobin MJ, Ratib S, Fielder AR. Change of refractive state and eye size in children of birth weight less than 1701 g. *Br J Ophthalmol.* 2006 Apr; 90(4):456-60.
14. Iwase S, Kaneko H, Fujioka C, Sugimoto K, Kondo M, Takai Y, et al. A long-term follow-up of patients with retinopathy of prematurity treated with photocoagulation and cryotherapy. *Nagoya J Med Sci* 2014; 76:121–8.

15. Zhu X, Zhao R, Wang Y, Ouyang L, Yang J, Li Y, Pi L. Refractive state and optical compositions of preterm children with and without retinopathy of prematurity in the first 6 years of life. *Medicine (Baltimore)*. 2017;96(45):e8565.
16. Xia YY, Gao X, Yin ZQ, Chen L, Liu Q, Chen X, et al. Refractive status and optical components in premature babies with and without retinopathy of prematurity at 5 years old. *Int J Clin Exp Med* 2017;10:3263–71
17. Fledelius HC. Myopia of prematurity, clinical patterns. *Acta Ophthalmol Scand* 1995; 73:402–6.
18. Quinn GE, Dobson V, Kivlin J, Kaufman LM, Repka MX, Reynolds JD, et al. Prevalence of myopia between 3 months and 5 1/2 years in preterm infants with and without retinopathy of prematurity. Cryotherapy for Retinopathy of Prematurity Cooperative Group *Ophthalmology*. 1998; 105:1292–300.
19. Holmstrom G, el Azazi M, Kugelberg U. Ophthalmological long term follow up of preterm infants: a population based, prospective study of the refraction and its development. *Br J Ophthalmol* 1998; 82:1265–71
20. Larsson EK, Rydberg AC, Holmstrom GE. A population-based study of the refractive outcome in 10-year-old preterm and full-term children. *Arch Ophthalmol* 2003; 121:1430–6.
21. Darlow BA, Elder MJ, Kimber B, Martin J, Horwood LJ. Vision in former very low birth weight young adults with and without retinopathy of prematurity compared with term born controls: the NZ 1986 VLBW follow-up study. *Br J Ophthalmol* 2018; 102(8):1041-1046.
22. Quinn GE, Dobson V, Davitt BV, Hardy RJ, Tung B, Pedroza C, et al; Early Treatment for Retinopathy of Prematurity Cooperative Group. Progression of myopia and high myopia in the early treatment for retinopathy of prematurity study: findings to 3 years of age. *Ophthalmology* 2008; 115(6):1058-1064.e1.
23. Quinn GE, Dobson V, Davitt BV, Wallace DK, Hardy RJ, Tung B, et al; Early Treatment for Retinopathy of Prematurity Cooperative Group. Progression of myopia and high myopia in the Early Treatment for Retinopathy of Prematurity study: findings at 4 to 6 years of age. *JAAPOS* 2013; 17(2):124-8.
24. Park JH, Chang YS, Ahn SY, Sung SI, Park WS. Predicting mortality in extremely low birth weight infants: Comparison between gestational age, birth weight, Apgar score, CRIB II score, initial and lowest serum albumin levels. *PLoS One* 2018; 13(2):e0192232.
25. Pan CW, Qian DJ, Zhu H, Yu JJ, Liu H. Apgar score and reduced vision in children aged 3 to 6 years. *Graefes Arch Clin Exp Ophthalmol* 2017; 255(2):401-405.
6. Fielder A, Blencowe H, O'Connor A, Gilbert C. Impact of retinopathy of prematurity on ocular structures and visual functions. *Arch Dis Child Fetal Neonatal Ed* 2015; 100(2):F179-84.
26. Fuchs F, Senat MV. Multiple gestations and preterm birth. *Semin Fetal Neonatal Med* 2016;21(2):113-20

27. Levy N, Shinwell ES, Leiba H. Long-term refractive status of preterm infants from singleton and multiple pregnancies. *J Matern Fetal Neonatal Med* 2017; 30(19):2276-2280.
28. Holmström GE, Kallen K, Hellstrom A, Jakobsson PG, Serenius F, Stjernqvist K, et al. Ophthalmologic outcome at 30 months' corrected age of a prospective Swedish cohort of children born before 27 weeks of gestation: the extremely preterm infants in Sweden study. *JAMA Ophthalmol* 2014; 132:182–9.
29. Quinn GE, Dobson V, Siatkowski R, Hardy RJ, Kivlin J, Palmer EA, et al; Cryotherapy for Retinopathy of Prematurity Cooperative Group. Does cryotherapy affect refractive error? Results from treated versus control eyes in the cryotherapy for retinopathy of prematurity trial. *Ophthalmology* 2001; 108:343–7.
30. Davitt BV, Quinn GE, Wallace DK, Dobson V, Hardy RJ, Tung B, et al; Early Treatment for Retinopathy of Prematurity Cooperative Group. Astigmatism progression in the early treatment for retinopathy of prematurity study to 6 years of age. *Ophthalmology* 2011; 118:2326–9.
31. Fieß A, Schuster AK, Nickels S, Elflein HM, Schulz A, Beutel ME, et al. Association of low birth weight with myopic refractive error and lower visual acuity in adulthood: results from the population-based Gutenberg Health Study (GHS). *Br J Ophthalmol* 2019;103(1):99-105.
32. Costeloe KL, Hennessy EM, Haider S, Stacey F, Marlow N, Draper ES. Short term outcomes after extreme preterm birth in England: comparison of two birth cohorts in 1995 and 2006 (the EPICure studies). *BMJ* 2012; 345:e7976.
33. Mutti DO, Sinnott LT, Lynn Mitchell G, Jordan LA, Friedman NE, Frane SL, Lin WK. Ocular Component Development during Infancy and Early Childhood. *Optom Vis Sci* 2018; 95(11):976-985.
34. Fledelius HC. Pre-term delivery and subsequent ocular development. A 7–10 year follow-up of children screened 1982–84 for ROP. 4) Oculometric—and other metric considerations. *Acta Ophthalmol* 1996; 74:301–5
35. Holmström G, Larsson E. Outcome of retinopathy of prematurity. *Clin Perinatol* 2013; 40:311–21.