

# Accepted Manuscript

## Myopia Progression in Low Birth Weight Infants: A Narrative Review

**Running title:** Myopia Progression

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## 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

ACCEPTED MANUSCRIPT (UNCORRECTED PROOF)

## 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]  $\leq 37$  weeks) is negatively correlated with GA and birth weight (3-6).

Refractive errors include myopia (spherical equivalent  $\geq -0.75$  diopters [D] extreme), high myopia (spherical equivalent  $\geq -6.00$  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 ( $\geq 1$  D cylinder and anisometropia ( $\geq 1$  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).

<b>Table 1.</b> 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 ( $\geq 2$ D to $< 6$ D): ▶ Treated eyes 20.5% ▶ Untreated eyes 15.5% High myopia ( $\geq 6$ 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.

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#### **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.

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