〈Review〉

Epidemiological Studies on Early-onset Myopia: A Review

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ABSTRACT The epidemiology of early-onset myopia has been investigated in terms of onset and progression with longitudinal (cohort) and cross-sectional studies. The majority of myopia in East Asia is early-onset myopia, which occurs in children, and the progression rate of myopia in myopic school children decreases with age. The onset of myopia at an earlier age is a predictive factor for future high-grade myopia, but the coefficient of determination is small. The worldwide increase in the prevalence of high myopia has led to a growing number of epidemiological studies that are directly related to myopia control studies, such as how to identify future high myopia at an early stage and how to predict myopia before its onset. We summarize the results from recent epidemiological studies.

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Key words：Epidemiological studies, Early-onset myopia, Myopia onset, Myopia progression, Children

INTRODUCTION

In 2015, a science writer in Boston, Dolgin, wrote an article in the journal Nature entitled "The myopia boom," in which he noted that the prevalence of myopia has increased uniformly around the world over the past 50 years as if it were an epidemic[1]. This trend can also be observed in the annual school health survey reported by the Japanese Ministry of Education, Culture, Sports, Science, and Technology (https://www.mext.go.jp/en/publication/index.htm) as shown in Fig. 1.

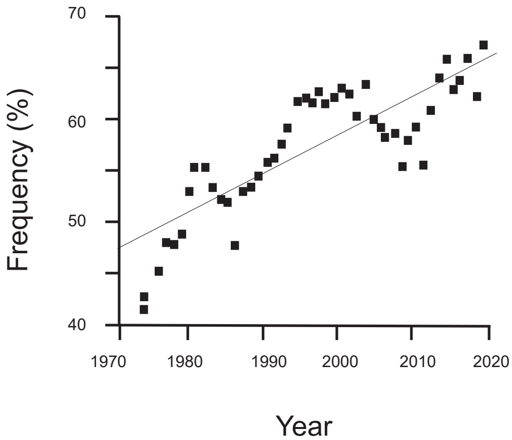

Fig. 1. Frequency of high school students with uncorrected visual acuity less than 1.0 (20/20).
regression line: y = 0.38x-718.

According to a simulation reported from the Brien Holden Institute[2], if no action is taken, the myopic population will increase rapidly, and the

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prevalence of high myopia globally, which was 2.7% (150 million people) in 2000, will increase to 9.8% (940 million people) in 2050. The prevalence of high myopia will increase by a factor of 5.8, which will lead to an increase in the number of serious eye diseases, such as macular degeneration, retinal detachment, and glaucoma, due to the extensive elongation of the eye associated high myopia. Accordingly, the burden on society and the medical economy will become enormous. Therefore, society needs to take comprehensive measures to control myopia progression in children.

Based on this awareness of the crisis, epidemiological studies on early-onset myopia have increased sharply around the world. This paper summarizes recent epidemiological research based on the White Paper published last year by the International Myopia Institute (IMI) in collaboration with the World Health Organization (WHO) (https://www.myopiainstitute.org/imi-white-papers.html).

EMMETROPIZATION AND MYOPIA PROGRESSION

The refractive errors in newborns vary widely among individuals and are normally distributed with a mean of mild hyperopia (+2 D). At 6 to 12 months of age, the hyperopia gradually decreases, and the distribution deviates from the Gaussian distribution and changes to a distribution with higher kurtosis. This phenomenon is known as emmetropization, which indicates that emmetropia is not congenital, but rather acquired as the child grows, depending on the visual environment[3].

Thereafter, hyperopia continuously decreases, and by the time the child is in elementary school, the refractive error is in the range of 0 to +2 D. In developing countries, the refractive error usually remains in this range until adulthood. In developed countries, however, for reasons that are not fully understood, myopia frequently develops and persists during childhood (early-onset myopia).

EPIDEMIOLOGY OF MYOPIA ONSET

The prevalence of myopia in children under 6 years of age is usually less than 5%, even in East Asian countries where it is highest[4]. However, in recent years it has been reported that the prevalence is increasing even in this age group. For example, the prevalence among young children (3-6 years old) in Hong Kong has doubled from 2.3% to 6.3% over the past 10 years[5]. The prevalence increases sharply after the age of six. Since this age coincides with the start of elementary school, it is considered that the visual burden of schooling may be the cause of myopia[6]. The annual incidence of myopia is constant between the ages of 7 and 15 in China, and by the age of 18, about 80% of children living in urban areas are myopic[7]. A similar trend is observed in Singapore, Hong Kong, Taiwan, Korea, and Japan, although the annual incidence decreased with age in the former three countries.

According to a meta-analysis reported by Rudnicka *et al.*[8], the prevalence of myopia in East Asia has increased by 23% over the past decade. Although the prevalence is also increasing in Europe and the United States, the incidence of myopia in childhood remains low, and late-onset myopia, which develops after the age of 16, accounts for the majority of the myopic population in the United Kingdom[9]. Fig. 2 shows the difference in the prevalence of myopia between East Asian and Western countries[10].

Flitcroft developed a mathematical model of myopia progression and predicted that since most infants have mild hyperopia, there is a transition period before the onset of myopia, and that there should be a difference in the reduction rate of hyperopia during this period between children who become myopic and those who remain emmetropic[11]. According to the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) study in children who had myopia, a rapid reduction in hyperopia and acceleration of ocular elongation were observed from four years

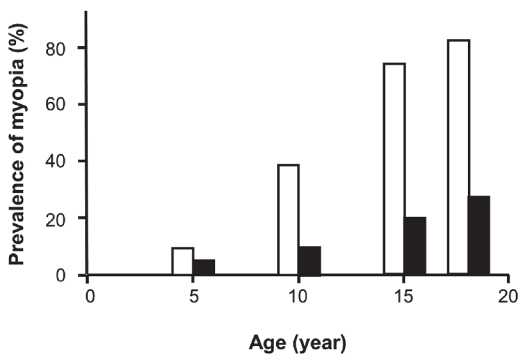

Fig. 2. Difference in the myopia progression between East Asian (white bars) and the Western (Caucasians, black bars) countries (a modified graph from Reference 10)

before the myopia onset and stabilized thereafter[12]. There have also been attempts to prevent the onset of myopia by predicting myopia onset based on biometrical parameters of the eye measured in early childhood.

EPIDEMIOLOGY OF MYOPIA PROGRESSION

The rate of myopia progression has been the subject of fewer epidemiological studies than those on incidence and prevalence. However, myopia control strategies should be developed in terms of both onset and progression. For this purpose, longitudinal (cohort) studies are ideal, but they are time- and cost-intensive. Cross-sectional studies are useful as long as they examine myopia progression rates evenly across a wide age range. In reality, information obtained from both types of studies is usually combined.

Donovan *et al*. conducted a meta-analysis based on previously reported longitudinal and cross-sectional studies of myopic schoolchildren of Asian and European descent living in urban areas (n = 2195)[13]. According to this analysis, the rate of myopia progression decreased with age, and the rate of the decrease also decayed with it (indicated by the open and closed circles in Fig. 3). For example, the myopia progression rate in Asian myopic schoolchildren was -1.12 D / year at age 7 and -0.50 D / year at age 12. However, this meta-analysis used data from a control group in an interventional clinical trial and was not necessarily representative of the general population.

The first community/school population-based study was conducted in China (n = 4662, mean baseline age: 9.8 years, follow-up: 2 years) and reported in 2002[14]. This study reported an average myopia progression rate of -0.35 D / year. In a cohort study in Hong Kong (n = 255, baseline age: 5 years, follow-up: 5 years), the average rate was -0.63 D / year. In the Singapore Cohort Of the Risk factors for Myopia (SCORM, n = 928, baseline age: 8 years, follow-up $\leq$ 11 years) study reported in 2016, the myopia progression rate was slightly slower than that from the meta-analysis by Donovan *et al.*[13], and the decrease in the progression rate did not decay with age (indicated by the squares in Fig. 3).

In a cohort study in Taipei reported in 2017 (n = 3256), myopic school children had a mean myopia progression rate of -0.42 D / year. However, the subjects included children treated with atropine eye drops. A school population-based study of children not receiving atropine eye drop treatment (n = 89)

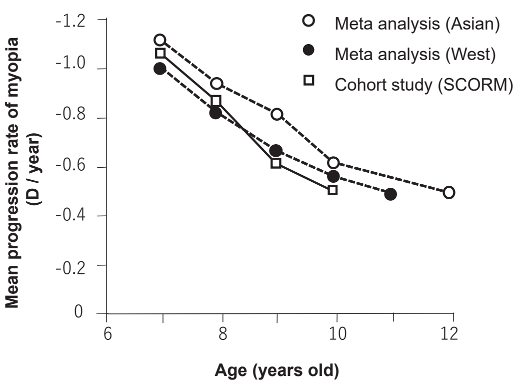

Fig. 3. Relationship between myopia progression rate per year and age (a modified graph from Reference 10)
The results of the meta-analysis by Donovan *et al.*[13] and the SCORM cohort study[15] were compared. The mean rate of myopia progression decreases with age.

showed a higher mean progression rate (-0.79 D / year).

As shown above, epidemiological studies vary in terms of their subjects, methods, and reporting formats. Therefore, comparison and integration are not easy. However, we can conclude that the rate of myopia progression in myopic children tends to decrease with age (growth). For parents who are concerned by myopia progression observed in their children, this may provide some modest evidence of comfort. In addition, since the growth curve of ocular axial length showed the same time-course as that of myopia, there have been attempts to predict myopia progression based on measurement of the axial length.

EPIDEMIOLOGY OF RISK FACTORS FOR PROGRESSING TO HIGH-GRADE MYOPIA

SCORM[15] is one of the few comprehensive epidemiological studies to address high-grade myopia. This study indicated that earlier onset of myopia is a risk factor for future high myopia. Eighty-seven percent of the high myopia cases had onset of myopia (persistent myopia progression for more than four years) before the age of seven. However, in a cohort study of the British population[16], Williams *et al*. concluded that the determinant coefficient of the age of onset on the degree of myopia in the future was only 15%, which is not necessarily a reliable indicator.

EPIDEMIOLOGY OF ADULTHOOD MYOPIA

Early-onset myopia usually ceases progression by the age of 14-17 years. In some cases, however, the progression continues into adulthood[17]. This is especially observed in those who have to do intensive near work during study or work or those who already have high myopia. Therefore, preventive treatments from a different perspective are required for these patients.

CONCLUSIONS

The IMI White Paper reported that myopia onset at an early age is a risk factor for high myopia. However, earlier-onset myopia does not always progress and become high-grade myopia. On the other hand, in some cases, myopia occurs after the age of 11 but progresses rapidly and still becomes high-grade myopia; therefore, we need to take such cases into account in clinics. When considering empirical knowledge of myopia progression, we can say that there are no surprising findings in recent epidemiological studies. However, most of these studies have conducted refractive examinations under cycloplegic conditions, so the level of evidence has certainly improved. It should be noted that the number of smartphone users has increased rapidly and remote learning through electronic devices has become more common due to the COVID-19 pandemic. There is also a concern that these changes in the visual environment surrounding children will affect the process of myopia progression.

An epidemiological study of childhood myopia will soon be launched by the Japan Ophthalmologists Association and the Japanese Ophthalmological Society, in collaboration with the Japanese Ministry of Education, Culture, Sports, Science, and Technology. Hopefully, this will establish further evidence for both onset and progression of myopia based on a solid research plan.

(This article is an English translation of a review paper published in Japanese[18].)

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