Original Article

Myopia progression in school children with prolonged screen time during the coronavirus disease confinement

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ABSTRACT

Background: Myopia, the most common refractive error, is a global public health problem with substantial visual impairment if left untreated. Several studies have investigated the association between increased near-work and restricted outdoor activities in children with myopia; however, such studies in children without myopia are scarce. We aimed to monitor the effect of the coronavirus disease-2019 (COVID-19) home confinement and mandatory virtual learning on myopic progression among myopic and non-myopic school-aged children.

Methods: We conducted a retrospective chart review of children aged 6 – 12 years attending regular visits to the pediatric ophthalmology clinic in a tertiary eye hospital in Eastern Province, Saudi Arabia. Cycloplegic refraction was determined from three visits at least six months apart: two visits before the start of the COVID-19 pandemic and one during the COVID-19 home confinement. Parents were asked about the time spent in near-work and outdoor activities, the devices used during virtual learning, and the demographic characteristics of the children. Statistical analyses were conducted to compare myopia progression before and during the COVID-19 home confinement.

Results: A total of 160 eyes of 80 children were analyzed. The boy (n = 46) to girl (n = 34) ratio was 1.4:1. The hyperopia (n = 131 eyes) to myopia (n = 29 eyes) ratio was 4.5:1. Most eyes exhibited a hyperopic shift before the confinement; however, all eyes displayed a myopic shift during the confinement. When comparing both eyes of the same individual, the more myopic or less hyperopic eye in the same child had a significantly greater myopic shift than the fellow eye (both $P < 0.05$). Children who used tablets showed a significant myopic shift ($P < 0.05$). Likewise, children in both age categories (≤ 8 and > 8 years), boys, those living in an apartment, and those having parents with bachelor's degrees experienced a significant myopic shift during COVID-19 home confinement compared to before (all $P < 0.05$). The mean myopic shift was greater in children aged > 8 years than in those aged ≤ 8 years. Children with and without a family history of myopia had a myopic shift in the mean spherical equivalent during COVID-19 home confinement; however, that of children with no family history was statistically significant ($P < 0.05$).

Conclusions: Progression of myopia accelerated in children during the COVID-19 pandemic. Excessive time spent on digital screen devices at near distances is considered a substantial environmental contributor to myopic shift in children. Further multicenter studies with extended follow-up periods are needed to assess the factors contributing to myopic progression in our population.

KEYWORDS

coronavirus disease 19, COVID-19 pandemic, online learning, distance education, refractive error, myopia, hypermetropia, children, clinical progression, health lockdown, visual acuity, ocular refraction

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How to cite this article: AlShamlan FT, Bubshait LK, AlAhmad EA, AlOtaibi BS, AlShakhs AA, AlHammad FA. Myopia progression in school children with prolonged screen time during the coronavirus disease confinement. Med Hypothesis Discov Innov Ophthalmol. 2023 Summer; 12(2): 90-97. https://doi.org/10.51329/mehdiophthal1474

Received: 03 November 2023; Accepted: 24 December 2023

INTRODUCTION

Myopia, the most common refractive error, is a global public health problem that leads to substantial visual impairment if left untreated [1]. It is influenced by hereditary and environmental factors [2]. Extended outdoor activities have been associated with a lower incidence of myopia; however, family history of myopia, near-work activities, and long study periods have been linked to myopia risk [3-5].

In light of the difficulty and ethical concerns associated with exposing children to prolonged screen time, a link between long-term exposure to digital device screens and myopia is disputed, with some studies supporting the link and others refuting it [6, 7]. However, the obligatory shift to online education during the coronavirus disease-2019 (COVID-19) home confinement provided an opportunity to study this in a real-life setting [8, 9]. During the COVID-19 pandemic, most countries implemented urgent measures to halt viral spread. Saudi Arabia implemented a variety of measures, including temporary home confinement that restricted outdoor activities, closure of schools, and transition to virtual education, which inevitably increased the use of digital devices [10].

Several studies have reported a substantial increase in the prevalence of myopia over the last few decades. According to the World Health Organization, 52% of the global population is expected to become myopic by the year 2050 [11]. Several studies have investigated the association between increased near-work and restricted outdoor activities in children with myopia; however, studies on the effects of these risk factors in children without myopia are scarce [4, 5, 12].

This study investigated the effects of the COVID-19 home confinement and mandatory virtual learning on myopic progression among myopic and non-myopic school-aged children.

METHODS

This retrospective chart review was conducted at Dhahran Eye Specialist Hospital (DESH), Dhahran, Saudi Arabia. The study included all eligible children aged 6 – 12 years who attended pediatric ophthalmology clinics at DESH between 2018 and 2021. In accordance with the Declaration of Helsinki, the ethics committee of the local institute approved the study, and the parents provided written informed consent. Children with any associated eye disease or a history of ocular surgery were excluded from analysis.

All eyes underwent pre-confinement cycloplegic refraction on two separate visits and one cycloplegic refraction during the COVID-19 home confinement. We retrospectively collected data from the cycloplegic refractions performed on three separate visits with a minimum of six-month intervals. The first refraction was conducted between August 2018 and July 2019. The second took place between September 2019 and February 2020, before the start of the COVID-19 home confinement in Saudi Arabia. The third was conducted between August 2020 and December 2021 during the school closure and home confinement [10].

Cycloplegia was induced by instilling a drop of 1% cyclopentolate ophthalmic solution (Cyclogyl; Alcon, Fort Worth, TX, USA) in each eye three times at 5-min intervals. Cycloplegic refraction was performed 30 min after the third instillation using a Heine Beta 200 Streak Retinoscope (HEINE Optotechnik, Herrsching, Germany) in a dimly lit room. All cycloplegic refractions were performed in the same setting under the same environmental conditions by an experienced full-time optometrist. Refraction results were recorded as the spherical component of the refractive error (sphere) in diopters (D), the cylindrical component of the refractive error (cylinder) in diopter cylinder (DC) and its axis direction, and the spherical equivalent of the refractive error (SE) in D.

All children underwent a complete ophthalmological examination, including measurement of best-corrected distance visual acuity using a Snellen chart (Auto Chart Projector CP 770; Nidek Co., Ltd., Gamagori, Japan), intraocular pressure measurement using an iCare portable handheld rebound tonometer (iCare Finland Oy, Vantaa, Finland), and undilated and dilated slit-lamp biomicroscopy examination (Photo-Slit Lamp BX 900; Haag-Streit, Koeniz, Switzerland) for anterior and posterior segment assessment.

The parents of 60 of the included children completed a telephone questionnaire in keeping with social distancing. We asked questions regarding average hours spent per day on near-work school activities, near-work non-school activities, and outdoor activities before and during the COVID-19 home confinement (< 1 h, 1–2 h, 2–4 h, 4–6 h, or > 6 h); type of devices used for virtual learning (television, personal computer, tablet, smartphone, or multiple devices) with time spent on each device (1–2 h, 2–4 h, 4–6 h, or > 6 h); and demographic data including age (≤ 8 years or > 8 years), sex (boy or girl), family size (no siblings, 1–2 siblings, or ≥ 3 siblings), dwelling unit (apartment or house), family history of myopia (positive or negative), and parents' education levels (pre-secondary school, secondary school, bachelor's degree, or higher education).

The outcome measure was SE, calculated as sphere power plus one-half the cylinder power. As per the International Myopia Institute, an SE ≤ - 0.5 D was considered myopia, and an SE + 0.5 D was considered

hyperopia [13]. In addition, myopic progression before and during the COVID-19 home confinement was measured as the following: *pre-confinement* = SE of second visit – SE of first visit, and *confinement* = SE of third visit – SE of second visit.

Statistical analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, version 22.0; Armonk, NY, USA). Normality of the data distribution was evaluated using the Shapiro – Wilk test. Continuous variables are presented as means and standard deviations (SDs). Categorical variables are presented as numbers and percentages. Statistical analysis was performed using the paired samples *t*-test or Wilcoxon signed-rank test, when applicable. A *P*-value < 0.05 was considered statistically significant.

RESULTS

We analyzed 160 eyes from 80 children with a mean (SD) age of 8.25 (2.35) years at the time of the first visit. The boy (n = 46, 57.5%) to girl (n = 34, 42.5%) ratio was 1.4:1. The mean (SD) follow-up interval between the three visits was approximately 11.0 (2.0) months.

The refractive error recorded during the first visit indicated that 18.1% (n = 29) of the eyes were myopic and 81.9% (n = 131) were hyperopic. A hyperopic shift was noted at the second visit, before the COVID-19 home confinement period. However, records from the third visit, after the COVID-19 home confinement, indicated a myopic shift. When comparing both eyes of the same individual, the more myopic and less hyperopic eyes had significantly more myopic shift than the fellow eye, showing significantly more myopic change in SE (both $P < 0.05$) (Table 1).

The devices used by the 60 children whose parents replied via phone interviews, in order of decreasing frequency, were tablets, smartphones, multiple devices, personal computers, and televisions. For those using multiple devices, the mean (SD, range) number of devices used was 1.45 (0.59, 1 to 3). We found a significant change in SE only in the eyes of individuals using tablets ($P < 0.05$) (Table 2), indicating a greater myopic shift when using this device during the COVID-19 home confinement. The percentages of time spent using devices significantly changed for all devices (all $P < 0.05$), except for television ($P > 0.05$), during the COVID-19 home confinement compared to the period before (Table 3).

There was a statistically significant increase in the time spent on near-work school activities ($P < 0.001$) and a decrease in outdoor activities ($P < 0.001$) during the COVID-19 home confinement compared to before, while that of near-work non-school activities remained unchanged ($P > 0.05$) (Table 4).

Children in both age categories (≤ 8 and > 8 years), boys, those living in an apartment, and those having parents with bachelor's degrees experienced a significant myopic shift during the COVID-19 home confinement compared to before (all $P < 0.05$). The mean myopic shift was greater in children aged > 8 years than in those aged ≤ 8 years (Table 5). Although we observed a myopic shift in the mean SE of the girls, this shift was not statistically significant ($P > 0.05$). Children with and without a family history of myopia had a myopic shift in the mean SE during the COVID-19 home confinement; however, that of children without a family history was statistically significant ($P < 0.05$). The change in SE during the COVID-19 home confinement versus pre-confinement was not statistically significant for the other factors listed in Table 5 (all $P > 0.05$).

The time spent on all devices did not differ between boys and girls before ($P = 0.297$) or during ($P = 0.356$) the COVID-19 home confinement. Likewise, the time spent on tablets did not differ between boys (58.3% for 1–2 h, 25.0% for 2–4 h, 16.7% for 4–6 h, and 0.0% for > 6 h) and girls (60.0% for 1–2 h, 26.7% for 2–4 h, 13.3% for 4–6 h, and 0.0% for > 6 h) before ($P = 0.843$) or between boys (9.1% for 1–2 h, 63.6% for 2–4 h, 18.2% for 4–6 h, and 9.1% for > 6 h) and girls (0.0% for 1–2 h, 53.3% for 2–4 h, 40.0% for 4–6 h, and 6.7% for > 6 h) during ($P = 0.131$) the COVID-19 home confinement. The correlation between age and changes in SE was not significant before confinement (r = - 0.09; $P = 0.266$), but became significant during the COVID-19 home confinement (r = - 0.27; $P = 0.001$).

DISCUSSION

This study revealed a substantial myopic shift in school-aged children who used tablets during the COVID-19 home confinement. The link between long-term exposure to digital device screens and myopia is debatable, with some studies supporting the link and others indicating the contrary [6, 7]. These studies were questionnaire-based and did not regularly expose children to prolonged screen time. However, the obligatory shift to online education during the COVID-19 pandemic has provided an opportunity to investigate this issue [8, 9]. Recently, multiple studies have been published on the effects of COVID-19 quarantine on myopic children [14-17]. Concerns about the potential progression of myopia during the COVID-19 pandemic escalated because of alterations in lifestyle brought on by home confinement, decreased outdoor activity, and virtual learning [18].

Table 1. Changes in SE in contralateral eyes before and during the COVID-19 home confinement, per refractive error magnitude

Category of refractive error	Changes in SE (D), Mean ± SD		*P*-value
	Pre-confinement	Confinement	
Less myopic eye, (n = 16)	-0.29 ± 0.45	-0.09 ± 0.82	0.615
More myopic eye, (n = 16)	+ 0.24 ± 1.15	-0.29 ± 1.30	**0.046**
Less hyperopic eye, (n = 64)	+ 0.19 ± 0.62	-0.20 ± 0.61	**0.001**
More hyperopic eye, (n = 64)	+ 0.08 ± 0.64	-0.04 ± 0.63	0.138

Abbreviations: SE, spherical equivalent of refractive error; COVID-19, coronavirus disease-2019; D, diopters; SD, standard deviation; n, number of eyes. Note: *P*-values < 0.05 are shown in bold; *P*-value is derived from the paired samples *t*-test; Minus sign (-) indicates myopic shift; Plus sign (+) indicates hyperopic shift; SE is calculated as spherical + 1/2 cylindrical components of refractive error in cycloplegic refraction; SE of ≥ - 0.5 D is considered myopia, and SE of ≥ + 0.5 D is considered hyperopia [13]; In this table, we compare the two eyes of one individual; if both are myopic, the more myopic eye is considered the one with an SE difference of ≥ - 0.5 D compared to the fellow eye; if both eyes are hyperopic, the more hyperopic eye is considered the eye with an SE difference of ≥ + 0.5 D compared to the fellow eye; Change in pre-confinement SE = SE of second visit – SE of first visit; Change in confinement SE = SE of third visit – SE of second visit.

Table 2. Changes in SE before and during COVID-19 home confinement, per device used

Type of Device	n (%)	Changes in SE (D), Mean ± SD		*P*-value
		Pre-confinement	Confinement	
Television	4 (3.3)	+ 0.19 ± 0.80	+ 0.25 ± 0.50	1.000
Personal computer	14 (11.7)	+ 0.28 ± 0.58	+ 0.02 ± 0.33	0.135
Tablet	54 (45.0)	+ 0.08 ± 0.68	-0.24 ± 0.59	**0.030**
Smartphone	28 (23.3)	+ 0.02 ± 0.99	-0.01 ± 1.26	0.330
Multiple devices	20 (16.7)	+ 0.05 ± 0.54	-0.10 ± 0.79	0.904

Abbreviations: SE, spherical equivalent of refractive error; COVID-19, coronavirus disease-2019; D, diopters; SD, standard deviation; n, number of eyes. Note: *P*-value < 0.05 is shown in bold; *P*-value is derived from the Wilcoxon signed-rank test; Parents of 60 children were interviewed via telephone; thus, the total number of eyes is 120; SE is calculated as spherical + 1/2 cylindrical components of refractive error in cycloplegic refraction; Change in pre-confinement SE = SE of second visit – SE of first visit; Change in confinement SE = SE of third visit – SE of second visit.

Table 3. Time spent on devices before and during COVID-19 home confinement

Type of Device	Status	Hours spent on devices				*P*-value
		1–2 h	2–4 h	4–6 h	> 6 h	
Television	**Pre-confinement**	100.0%	0.0%	0.0%	0.0%	0.157
	Confinement	50.0%	50.0%	0.0%	0.0%	
Personal computer	**Pre-confinement**	100.0%	0.0%	0.0%	0.0%	**0.003**
	Confinement	0.0%	80.0%	20.0%	0.0%	
Tablet	**Pre-confinement**	59.3%	25.9%	14.8%	0.0%	**< 0.001**
	Confinement	3.8%	57.7%	30.8%	7.7%	
Smartphone	**Pre-confinement**	50.0%	28.6%	21.4%	0.0%	**< 0.004**
	Confinement	0.0%	58.3%	12.5%	29.2%	
Multiple devices	**Pre-confinement**	10.0%	40.0%	50.0%	0.0%	**0.023**
	Confinement	0.0%	11.1%	77.8%	11.1%	

Abbreviations: COVID-19, coronavirus disease-2019. Note: *P*-values < 0.05 are shown in bold; *P*-value is derived from the Wilcoxon signed-rank test; Pre-confinement, before COVID-19 pandemic; Confinement, during COVID-19 home confinement.

Nevertheless, few studies have raised these concerns in children with hyperopia in addition to myopia [12, 19]. To our knowledge, the current study is the first to analyze the effects of the COVID-19 home confinement on both myopic and hyperopic children in Saudi Arabia.

We observed a substantial myopic shift in school-aged children using tablets, but not in those using other devices, including televisions, personal computers, and smartphones. This is consistent with the findings of Ma et al. [14], who reported that myopia progression was slower in students using televisions and projectors than in those using mobile phones and tablets. They recommended the use of projectors and televisions instead of smartphones and tablets for online learning. They proposed that devices with shorter viewing distances would necessitate greater accommodation effort, resulting in greater myopic progression [14]. Ip et al. [6] reported that

Table 4. Comparison of times spent in near-work school, near-work non-school, and outdoor activities before and during COVID-19 home confinement

Type of Activity	Status	Hours spent for activity					*P*-value
		< 1 h	1–2 h	2–4 h	4–6 h	> 6 h	
Near-work school activities	**Pre-confinement**	57.6%	30.5%	11.9%	0.0%	0.0%	**< 0.001**
	Confinement	1.9%	1.9%	35.8%	50.9%	9.4%	
Near-work non-school activities	**Pre-confinement**	37.5%	25.0%	16.1%	7.1%	14.3%	0.158
	Confinement	38.9%	25.9%	22.2%	3.7%	9.3%	
Outdoor activities	**Pre-confinement**	42.6%	40.7%	11.1%	5.6%	0.0%	**< 0.001**
	Confinement	69.8%	24.5%	5.7%	0.0%	0.0%	

Abbreviations: COVID-19, coronavirus disease-2019. Note: *P*-values < 0.05 are shown in bold; *P*-value is derived from the Wilcoxon signed-rank test; Pre-confinement, before COVID-19 pandemic; Confinement, during COVID-19 home confinement.

Table 5. Factors associated with changes in SE before and during COVID-19 home confinement

Factors	Level	n	Change in SE (D), Mean ± SD		*P*-value
			Pre-confinement	Confinement	
Age	**≤ 8 years**	90	+ 0.18 ± 0.72	+ 0.02 ± 0.77	**0.024**
	> 8 years	70	+ 0.00 ± 0.65	-0.34 ± 0.63	**0.004**
Sex	**Boys**	92	+ 0.13 ± 0.66	-0.15 ± 0.71	**0.001**
	Girls	68	+ 0.06 ± 0.74	-0.11 ± 0.76	0.085
Family size	**No siblings**	10	+ 0.25 ± 0.63	-0.22 ± 0.93	0.259
	1-2 siblings	50	+ 0.15 ± 0.76	-0.03 ± 0.81	0.063
	≥ 3 siblings	60	+ 0.01 ± 0.72	-0.13 ± 0.75	0.157
Dwelling unit	**Apartment**	60	+ 0.11 ± 0.69	-0.02 ± 0.69	**0.049**
	House	60	+ 0.07 ± 0.77	-0.17 ± 0.88	0.136
Family history of myopia	**Positive**	46	+ 0.07 ± 0.90	-0.10 ± 0.92	0.325
	Negative	74	+ 0.10 ± 0.61	-0.09 ± 0.70	**0.015**
Fathers' education	**Pre-secondary school**	10	+ 0.08 ± 1.12	+ 0.22 ± 1.40	0.866
	Secondary school	34	+ 0.18 ± 0.80	-0.01 ± 0.79	0.061
	Bachelor's degree	60	+ 0.10 ± 0.65	-0.19 ± 0.75	**0.040**
	Higher education	16	-0.16 ± 0.62	-0.07 ± 0.36	0.571
Mothers' education	**Pre-secondary school**	14	-0.12 ± 0.83	+ 0.26 ± 0.98	0.689
	Secondary school	18	-0.03 ± 0.86	+ 0.24 ± 0.98	0.981
	Bachelor's degree	78	+ 0.17 ± 0.70	-0.17 ± 0.69	**0.009**
	Higher education	10	-0.32 ± 0.39	-0.45 ± 0.54	0.439

Abbreviations: SE, spherical equivalent; COVID-19, coronavirus disease-2019; D, diopters; SD, standard deviation; n, number of eyes. Note: *P*-values < 0.05 are shown in bold; P-value is derived from the paired samples t-test; The parents of 60 children were interviewed via telephone; thus, the total number of eyes is 120 except for variables of age and sex; SE, is calculated as spherical + 1/2 cylindrical components of refractive error in cycloplegic refraction; Change in pre-confinement SE = SE of second visit – SE of first visit; Change in confinement SE = SE of third visit – SE of second visit.

more time spent reading at a distance of less than 30 cm was linked to greater myopic refraction in Australian children. According to the Singapore Cohort Study of the Risk Factors of Myopia [20], myopia is more prevalent in children who read more than two books per week. Huang et al. [4] conducted a meta-analysis and observed that the probability of myopia increased by 2% with every diopter-hour spent on near-work activities per week [4]. In this study, we found a substantial increase in the time spent in near-work school-related activities during the COVID-19 home confinement. During the pre-confinement period, 57.6% of the children spent < 1 h on school-related near-work activities; however, after confinement, half of the children spent approximately 4–6 h.

Our findings support the substantial effects of risk factors for myopia during the pandemic, even in individuals with hyperopia. A hyperopic shift was observed in children before the COVID-19 home confinement; however, a myopic shift was detected after confinement. When both eyes of the same individual were compared, the more myopic and less hyperopic eyes showed a substantially greater myopic shift. This can be attributed to the fact that the eye with less hyperopic refraction is more prone to myopic progression [21, 22]. We found no studies comparing the progression of myopia in both eyes of the same individual during the COVID-19 pandemic.

According to Alvarez-Peregrina et al. [12], a decrease in SE was found in Spanish children when examined after the COVID-19 home confinement in comparison with the results in 2019, which indicates higher rates of myopia in children. They found that the percentage of hyperopes decreased and that of emmetropia increased, but the percentage of myopes was the same, considering that the children were evaluated using non-cycloplegic refraction. They linked myopia progression to limited time spent in outdoor activities. Wang et al. reported a substantial increase in the prevalence of myopia among young Chinese children during the COVID-19 home confinement [16]. They used the "photo-screening" test to measure non-cycloplegic refraction in more than 1000 children and compared results from the year 2020 with the those of the previous five years. Both photo-screening-based devices and non-cycloplegic refraction can overestimate results [23, 24]. In contrast to our study, theirs only included non-cycloplegic refraction results [16], and cycloplegic examination is the reference standard in studies on refractive errors in children [25].

In our study, children in both age categories (≤ 8 and > 8 years), boys, those living in an apartment, and those having parents with bachelor's degrees experienced a substantial myopic shift during the COVID-19 home confinement. The mean myopic shift was greater in children aged > 8 years than in those aged ≤ 8 years. Although we observed a myopic shift in the mean SE of the girls, it was not statistically significant. With regard to sex differences as a risk factor, the observations of Reed et al. [26] are consistent with our finding that myopia was significantly associated with male sex. However, other studies have found that the risk of myopia is higher in female individuals [27, 28].

Many studies have identified family history as a significant factor in myopia [29, 30]. However, the evidence showed that parental myopia may contribute to myopia in children by setting up a more myopic baseline at preschool age, and that it was not associated with a more myopic refractive shift [31], which concurs with our findings. However, there are potential racial/ethnic differences in the relative contributions of genetic and environmental factors to myopia [31, 32]. We found that children with and without a family history of myopia had a myopic shift in the mean SE during the COVID-19 home confinement, but that of children without a family history was statistically significant. Therefore, similar studies in our population are warranted to explain the observed discrepancies with other findings in the literature.

Childhood exposure to constricted living spaces is a well-known environmental risk factor for myopia development, and this effect was exaggerated by obligatory home confinement and restricted outdoor activities during the COVID-19 pandemic [33, 34]. Several studies analyzed the correlation between myopia prevalence and educational attainment [35, 36]. In the present study, children of parents with bachelor's degrees experienced a substantial myopic shift during the COVID-19 home confinement, which was attributed to the extended time spent on tablet devices as compared to that of other children. The Genes in Myopia Twin Study [35] reported that higher educational attainment is associated with a higher prevalence of myopia. In addition, according to Pan et al. [36], higher education is an independent risk factor for myopia development and is associated with longer axial lengths in Asian children. This may be correlated to more hours spent on reading and near-work activities.

To our knowledge, this study is the first to analyze the effects of the COVID-19 home confinement on both myopic and hyperopic children in Saudi Arabia. However, recruitment of a limited number of children, especially myopic children, and having a retrospective design, are among the limitations of this study. Prospective studies with extended follow-up periods, including ocular biometry data such as axial length and corneal curvature, could further assess the factors leading to the progression of myopia in our population.

CONCLUSIONS

Children in both age categories, boys, those living in an apartment, those without a family history of myopia, and those having parents with bachelor's degrees, experienced a substantial myopic shift during the COVID-19 home confinement. We observed that the extensive use of digital screen devices and increased near-work activities for online learning during the COVID-19 home confinement may have accelerated the progression of myopia. This study offers new perspectives on myopia management in clinical practice and increases our understanding of myopia progression. Further multicenter studies with extended follow-up periods are needed to assess the factors contributing to myopic progression in our population.

ETHICAL DECLARATIONS

Ethical approval: In accordance with the Declaration of Helsinki, the ethics committee of the local institute approved the study, and the parents provided written informed consent.

Conflict of interest: None.

FUNDING

None.

ACKNOWLEDGMENTS

None.

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