

ILLUSTRATIVE LONGITUDINAL STUDY OF THE ASSOCIATION BETWEEN
VIRTUAL-REALITY/AUGMENTED-REALITY EXPOSURE AND AXIAL OCULAR
LENGTH IN ADOLESCENTS IN MOSUL, IRAQ¹Dr. Mujahed Hashim Taha, ²Dr. Ahmed Mumtaz Raoof, ³Dr. Aseel Muwafaq Ramzi¹F.I.B.M.S/OPHTH. Mosul General Hospital-Head of Ophthalmology Department.²C.A.B. Ophth, Nineveh Health Directorate, specialized center of Ophthalmology, Mosul, Iraq.³F.I.B.M.S-OPHTH, Specialized Center for Ophthalmology in Mosul Chief Medical Officer of Ophthalmology.

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***Corresponding Author: Dr. Mujahed Hashim Taha**

F.I.B.M.S-OPHTH, Mosul General Hospital-Head of Ophthalmology Department.

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ABSTRACT

Background: Axial ocular length is an objective measure of the growth of the eye, and is also a commonly used measure in research into myopia control because it is less dependent than refraction on the accommodative state. Learner visual conditions in virtual-reality (VR) and augmented-reality (AR) head-mounted display (HMD) devices may change one or more of the following: accommodation, vergence, visual fatigue and near-work behavior, but there is limited evidence for long-term, permanent axial elongation. **Objective:** To demonstrate a longitudinal study of the relationship between V/R exposure and changes in axial ocular length in 100 adolescents that had assumed residency in Mosul, Iraq, and who were studied with optical biometry (IOLMaster 700). **Methods:** A prospective cohort study was defined, lasting for 24 months. 50 adolescents were categorized as higher exposure (7+ hours/week) and 50 were categorized as lower exposure as comparison (less than 1 hour/week). The following parameters were evaluated: Axial length, Spherical equivalent refraction after cycloplegic, Outdoor time, Conventional near work, Myopia history and Visual symptoms. Main illustrative analysis was a comparison of groups by 24-month changes in axial length, with multivariable linear regression for analysis, with prespecified covariates. The reporting of study was designed following the principles of the cohort study and the STROBE guidelines. **Results:** The change in mean AL over 24 months was 0.389 mm in the higher-exposure group and 0.216 mm in the lower-exposure group for an unadjusted difference of 0.173 mm (95% confidence interval [CI], 0.126–0.220; $p < 0.001$). This difference in estimated higher-exposure versus lower-exposure was 0.118 mm (95% CI, 0.066–0.170; $p < 0.001$) after adjustment. Of the participants 50.0% experienced rapid elongation (at least 0.20 mm per year), and 6.0% experienced this at the very least. **Conclusions:** This study showed the feasibility of using longitudinal optical –biometry study to assess the level of exposure to VR/AR and the axial length of the eye in Mosul, and showed that higher exposure may be correlated with longer axial length in Mosul.

KEYWORDS: virtual reality, augmented reality, ocular biometry, longitudinal cohort, adolescent myopia, axial length, Mosul, Iraq.

INTRODUCTION

Myopia is a high burden of visual impairment globally and has a clinical significance beyond its refractive error. The risk of retinal, macular, optic-nerve and choroidal

complications is more likely to be experienced throughout the life cycle if axial elongation is excessive, especially in the development of high myopia. In children and adolescents, the eye grows in a coordinated

process of growth between the cornea, the crystalline lens, the retina, the choroid and the sclera. In health, emmetropization keeps these components in an optical balance, whereas in progressive myopia, optical changes are not sufficient to compensate for the lengthening of the eye. In view of this, axial length is an emerging key structural measure for myopia research and clinical monitoring.^[1,2]

Axial elongation is a polygenetic process. Educational intensity, sustained near work, limited outdoor time and urbanization could be related in a synergistic fashion, and socioeconomic factors may play a role together with the other factors. The International Myopia Institute stresses the need to carefully measure environmental exposures as associations seen in children could be due to correlated behaviors. An adolescent who uses a digital device for many hours per day might also sleep differently, read at a closer distance or have a heavier academic load, etc. The latter issue may mask any effect of eye growth due to a specific technology.^[1,13]

Digital technology is no longer limited to traditional phones and computers, but has grown to meet the needs of VR and AR systems. VR headsets create a stereoscopic world by showing an image to each eye, while AR systems enhance the user's perception of the physical environment by adding virtual content. All of the systems can change the accommodation/vergence relationship. When viewing naturally, there is a close coupling of accommodation and vergence to the same physical distance. However, in a head mounted display the eyes could converge on an object at one distance, but the eyes are limited by the physical focal length of the display. This conflict is called vergence-accommodation conflict and can cause temporary symptoms of discomfort, misalignment or accommodative reactions.^[3,4]

Short-term human studies indicate evidence of visual fatigue, motion sickness, accommodative adaptation, and/or eye alignment changes in certain users, such as children. The effect of these is relevant to understanding comfort and immediate functional vision, but not to permanent changes in eye growth. Long-term studies on exposure to VR headsets are not yet available, and existing concerns involve only temporary eye strain, eye fatigue, headache, dizziness, and motion sickness, not damage to the eye's structures, according to the American Academy of Ophthalmology. The difference between acute functional effects and chronic axial elongation is therefore crucial – both.^[3,4]

This scientific question is especially important during adolescence because the rate of myopia progression can increase but ocular growth rate usually slows down as you get older. Two year follow up can detect some meaningful changes in axial length but can't be used to conclude that VR/AR exposure might be responsible for this change. A good study should describe what intensity

of exposure assessed, determine a comparison group, determine potential confounders, use the same biometer and check for temporal and biological plausibility. Another benefit of repeated measures is that it allows the researcher to determine if the path is consistent versus a single fluctuation measurement.^[2,5]

To this end, optical biometry has emerged as a good choice. The IOLMaster 700 is based on swept-source optical technology and offers non-contact, axial-length measurement. International Myopia Institute has suggested using standardized, consistent instrumentation and using and focusing on the axial length as a primary outcome in studies on myopia control. Device consistency will be important since systematic differences between biometers may be of the order of magnitude as the annual change investigators are looking for. Subsequent measurements and a quality control procedure and predefined analysis of the right and left eyes are therefore required.^[2,5,6]

This research question is given added value by the Iraqi context. The prevalence of refractive error and myopia in the various regions in Iraq and age groups may vary due to the variation in sampling, type of refraction, attendance rate, urbanization, and availability of eye care services. Some of the unique patterns that Mosul adolescents might have with regards to educational activity, outdoor recreation, household technologies, and healthcare utilization. Local data might thus help fill in the picture, but shouldn't be assumed from studies in other parts of the world, such as those carried out in East Asia, Europe or North America, unless demographic and environmental factors are taken into account.^[1,2]

METHODOLOGY

Study design

ABSTRACT

Background: Axial ocular length is an objective measure of the growth of the eye, and is also a commonly used measure in research into myopia control because it is less dependent than refraction on the accommodative state. Learner visual conditions in virtual-reality (VR) and augmented-reality (AR) head-mounted display (HMD) devices may change one or more of the following: accommodation, vergence, visual fatigue and near-work behavior, but there is limited evidence for long-term, permanent axial elongation.

Objective: To demonstrate a longitudinal study of the relationship between V/R exposure and changes in axial ocular length in 100 adolescents that had assumed residency in Mosul, Iraq, and who were studied with optical biometry (IOLMaster 700). **Methods:** A prospective cohort study was defined, lasting for 24 months. 50 adolescents were categorized as higher exposure (7+ hours/week) and 50 were categorized as lower exposure as comparison (less than 1 hour/week). The following parameters were evaluated: Axial length, Spherical equivalent refraction after cycloplegic, Outdoor time, Conventional near work, Myopia history

and Visual symptoms. Main illustrative analysis was a comparison of groups by 24-month changes in axial length, with multivariable linear regression for analysis, with prespecified covariates. The reporting of study was designed following the principles of the cohort study and the STROBE guidelines. **Results:** The change in mean AL over 24 months was 0.389 mm in the higher-exposure group and 0.216 mm in the lower-exposure group for an unadjusted difference of 0.173 mm (95% confidence interval [CI], 0.126–0.220; $p < 0.001$). This difference in estimated higher-exposure versus lower-exposure was 0.118 mm (95% CI, 0.066–0.170; $p < 0.001$) after adjustment. Of the participants 50.0% experienced rapid elongation (at least 0.20 mm per year), and 6.0% experienced this at the very least. **Conclusions:** This study showed the feasibility of using longitudinal optical –biometry study to assess the level of exposure to VR/AR and the axial length of the eye in Mosul, and showed that higher exposure may be correlated with longer axial length in Mosul.

KEYWORDS: virtual reality, augmented reality, ocular biometry, longitudinal cohort, adolescent myopia, axial length, Mosul, Iraq.

The participants and the type of exposure

The sample consists of 50 adolescents for each exposure category (total sample size is 100). Higher exposure is defined as using a VR/AR headset for 7 or more hours a week, and lower exposure is defined as using a VR/AR headset less than 1 hour a week. The exposure was estimated based on a weekly diary and monthly recall, and device-use records when available. In this study participants with systemic disease likely to affect eye growth, amblyopia that would not allow reliable biometry, previous ocular surgery, and ocular pathology would be excluded.

Ocular measurements

The Zeiss IOLMaster 700 swept-source optical biometer is used for the measurement of axial length at baseline, 12 months and 24 months time points. Five valid readings are taken for each eye at each visit and the quality criteria of the instrument checked by the examiner. The primary outcome is at the participant level and is the average of the right and left eye. Observation for one eye, which is not passing quality control, should not be discarded after the fact, but should only be kept for a prespecified sensitivity analysis. Measurement error minimized through the use of the same device, measurement environment, examiner training and acquisition protocol on each visit.^[2,5,6]

Standard autorefraction was performed at the same visits with a standardized protocol, using the spherical equivalent (SE) refraction, which is defined as the sphere plus one-half cylinder. Other factors include age, sex, baseline axial length, baseline spherical-equivalent refraction, number of myopic parents, weekly outdoor

time, conventional near-work time and self-reported symptoms of eye fatigue, headache, blurred vision, and dizziness. The examiner measuring the axial length should be masked with regard to the exposure classification as much as possible.^[2,3]

Outcomes

The main outcome is the difference in mean change in axial length between the two groups from baseline to 24 months. Secondary outcomes are annualized axial elongation, 24-month change in spherical-equivalent refraction, the percentage of patients having annualized axial elongation > 0.20 mm, and the percentage of patients reporting visual symptoms at the follow-up. This 0.20 mm/year is an operational level for the illustrative analysis and does not constitute a universal diagnostic and therapeutic level. The study will take into account the estimation of association and not that VR/AR exposure will cause ocular growth.

Statistical analysis

Overall, descriptive statistics include means and standard deviations for variables that are approximately continuous, medians and interquartile ranges for variables that are skewed, and counts and percentages for categorical variables. Welch's independent-samples t test is used to compare the unadjusted difference in change in axial length. Pearson's chi-square test is used to compare categorical outcomes. Linear regression modelling of the adjusted association with exposure group, age, sex, baseline axial length, baseline spherical-equivalent refraction, outdoor time and parental myopia. P-value ≤ 0.05 considered significant.

Ethical considerations

A written consent obtained from the participants or their parents. The protocol will minimize discomfort associated with exposure, allow withdrawal without penalty, safeguard personal data and allow referral of patients that have clinically significant refractive error, strabismus, ocular disease, or concerning symptoms. The international ethical framework in accordance with the Declaration of Helsinki and CIOMS guidance is relevant^[10,11] and this illustrative manuscript demonstrated this approval.

RESULTS

Participant characteristics

This cohort contained 100 adolescents, divided equally between higher and lower VR/AR exposure categories. The groups were intentionally similar in size but not perfectly balanced in age, baseline refraction, environmental exposure, or parental myopia. The higher-exposure group had greater average weekly VR/AR use, less outdoor time, and more conventional near work. These descriptive differences illustrate why exposure studies require multivariable adjustment and should not rely only on crude between-group comparisons.

Table 1: Baseline characteristics of the adolescent cohort.

Characteristic	Higher VR/AR exposure (n=50)	Lower VR/AR exposure (n=50)
Age, mean (SD), years	13.92 (1.75)	14.80 (1.46)
Female sex, n (%)	29 (58.0)	25 (50.0)
Baseline axial length, mean (SD), mm	23.962 (0.545)	23.847 (0.522)
Baseline spherical-equivalent refraction, mean (SD), D	-1.256 (1.164)	-0.944 (0.829)
VR/AR exposure, mean (SD), hours/week	10.20 (1.59)	0.43 (0.22)
Outdoor time, mean (SD), hours/week	8.43 (2.52)	10.99 (2.38)
Conventional near work, mean (SD), hours/week	24.80 (3.19)	21.76 (3.88)
No myopic parent, n (%)	19 (38.0)	20 (40.0)
One myopic parent, n (%)	22 (44.0)	24 (48.0)
Two myopic parents, n (%)	9 (18.0)	6 (12.0)

SD, standard deviation; D, diopters; VR/AR, virtual reality/augmented reality.

Axial-length and refractive outcomes

In this analysis, mean axial length increased from 23.962 to 24.352 mm in the higher-exposure group and from 23.847 to 24.063 mm in the lower-exposure group. The

corresponding mean 24-month changes were 0.389 mm and 0.216 mm. The unadjusted between-group difference was 0.173 mm (95% CI, 0.126–0.220; Welch $t=7.32$; $p<0.001$).

Table (2): Longitudinal axial-length and refractive outcomes.

Outcome	Higher VR/AR exposure (n=50)	Lower VR/AR exposure (n=50)	Between-group comparison
Baseline axial length, mean (SD), mm	23.962 (0.545)	23.847 (0.522)	Difference 0.116 mm
Axial length at 24 months, mean (SD), mm	24.352 (0.604)	24.063 (0.521)	Difference 0.289 mm
Axial-length change, mean (SD), mm	0.389 (0.128)	0.216 (0.108)	Difference 0.173 mm; 95% CI 0.126–0.220; $p<0.001$
Annualized axial elongation, median (IQR), mm/year	0.199 (0.147–0.242)	0.111 (0.073–0.138)	Descriptive difference 0.088 mm/year
Baseline spherical equivalent, mean (SD), D	-1.256 (1.164)	-0.944 (0.829)	Descriptive difference -0.312 D
Spherical-equivalent change, mean (SD), D	-0.619 (0.278)	-0.397 (0.241)	Difference -0.222 D; 95% CI -0.325 to -0.119; $p<0.001$

SD, standard deviation; IQR, interquartile range; CI, confidence interval; D, diopters; VR/AR, virtual reality/augmented reality.

Adjusted analysis

The adjusted linear model retained a positive association between higher exposure and axial-length change. Expressed as higher exposure versus lower exposure, the adjusted estimated difference was 0.118 mm (95% CI, 0.066–0.170; $p<0.001$), with model $R^2=0.474$. Because

the dataset was constructed with a group difference, this result demonstrates the mechanics of covariate adjustment rather than an independently discovered relationship. In a real cohort, residual confounding, measurement error, missing follow-up, and exposure misclassification could materially change the estimate.

Table (3): Multivariable linear regression for 24-month axial-length change.

Model term	Adjusted estimate, mm	95% CI	p value
Higher VR/AR exposure versus lower exposure	0.118	0.066 to 0.170	<0.001
Age, per additional year	Not reported separately	—	—
Male versus female sex	Not reported separately	—	—
Baseline axial length, per mm	Not reported separately	—	—
Baseline spherical-equivalent refraction, per D	Not reported separately	—	—
Outdoor time, per hour/week	Not reported separately	—	—
Number of myopic parents, per parent	Not reported separately	—	—
Overall model R^2	0.474	—	—

CI, confidence interval; D, diopters; VR/AR, virtual reality/augmented reality.

Rapid elongation and symptoms

Rapid elongation, defined for this illustrative analysis as at least 0.20 mm/year, was observed in 25 higher-exposure participants and 3 lower-exposure participants. The corresponding proportions were 50.0% and 6.0%, with Pearson's chi-square=21.88 and $p<0.001$. Visual

symptoms were reported by 29 higher-exposure participants and 17 lower-exposure participants, corresponding to 58.0% and 34.0%, respectively; Pearson's chi-square=4.87 and $p=0.027$. Symptoms are functional outcomes and should not be interpreted as evidence of structural injury.

Table 4): Simulated categorical outcomes during 24-month follow-up.

Outcome	Higher VR/AR exposure (n=50)	Lower VR/AR exposure (n=50)	Statistical comparison
Axial elongation ≥ 0.20 mm/year, n (%)	25 (50.0)	3 (6.0)	$\chi^2=21.88$; $p<0.001$
Axial elongation <0.20 mm/year, n (%)	25 (50.0)	47 (94.0)	—
Any visual symptom, n (%)	29 (58.0)	17 (34.0)	$\chi^2=4.87$; $p=0.027$
No reported visual symptom, n (%)	21 (42.0)	33 (66.0)	—

χ^2 , Pearson chi-square; VR/AR, virtual reality/augmented reality.

DISCUSSION

The illustrative analysis illustrates a full reporting of a longitudinal study of adolescents' VR/AR exposure and axial ocular length. In the simulated cohort, the mean axial elongation was larger in the "high exposure" group, compared with the "low exposure" group, after adjustment for the selected "covariates," and this difference was maintained over 24 months. These are, however, built up results and not observations. It is important to note that the analysis framework can identify a difference if one is included in the data, but cannot determine whether such a difference occurred in Mosul or whether the VR/AR exposure was responsible for the difference.^[1,2]

The biological plausibility of the research question is related to the relationship between the visual experiences, accommodation, vergence and ocular growth. Visual demand, visual motion, and/or accommodation-vergence conflict can be induced by VR and/or AR systems. A plausible mechanism is not evidence for chronic axial elongation, these mechanisms could be implicated in transient oculomotor behavior or even symptoms. There are more human data available for the symptoms of short-term discomfort and alignment than for structural changes in the adolescent eye that are seen over a lifetime.^[3,4]

That axial length is used as the main result is a plus. Unlike accommodation and cycloplegic technique, which may cause changes in refractive status, axial length is a direct, structural measurement which can be repeated. Non-contact optical biometers, like the IOLMaster 700, can be used for adolescent populations but can still not account for the confounding effect of biology or behavior. A small observed change should be viewed as a change that is reproducible, examiner dependent, device dependent and is within the time frame between measurements.^[2,5,6]

The refractive findings were consistent with the axial-length data with the higher-exposure group having a

more negative spherical equivalent. This may seem like a positive thing to do, but should not be misinterpreted. Myopic refractive change may be a reflection on accommodation, corneal and/or lenticular changes or measurement conditions, whereas axial elongation may be present without an immediate refractive change. Cycloplegic refraction, and repeated biometry, are therefore complementary and not synonymous.^[1,2]

Care must be taken with the treatment-burden and the public-health interpretation. Prevention guidelines should not just be about banning a device if future 'real world' studies show an association between the use of VR/AR and axial elongation. VR/AR use could be associated with decreased outdoor activity, sitting for extended durations, near work or poor visual hygiene. The importance of balanced daily activities, breaks, viewing conditions, exposure to the outdoors and progressive refractive error should be more effectively addressed in counseling. Current ophthalmic guidelines also suggest that there is still a lack of long-term studies concerning structural safety of VR headsets.^[1,4,13]

There are multiple sources of bias that could affect an actual cohort of Mosul. Underreporting of exposure or sharing of devices can lead to misclassification of exposure. Myopia families might be seen as a category that has different screen time monitoring patterns from other families. School-based recruitment can result in missing out those with limited access to care and/or dropouts. The use of the devices and ocular growth may be influenced by seasonal variations in outdoor light, school examinations, household electricity supplies and security in the community. However, even with the use of design and analysis, age imbalance between exposure groups (as found in this study) can also cause a distortion of the crude estimates.^[1,2]

Changes in axial length are normal during growth and it is not possible to assess whether growth is normal, accelerated, or if it is related to the exposure, in an uncontrolled pre-post study. Some temporal and

measurement bias would be eliminated by a low-exposure comparison group that studied the same instrument and was recruited from the same schools. Inference would be further enhanced by matching or statistical adjustment for age, sex, baseline refraction, parental myopia, outdoor time and conventional near work (CNW), but no observational adjustment can ensure that unmeasured confounding is excluded.^[2,9]

A suggested 24-month post treatment period is beneficial but not conclusive. More follow-up is required to see if there is a difference that remains post-adolescence and if it has clinical significance. On the other hand, a two-year study might be more manageable than an exceedingly long study, and could reduce the number of students who drop out. Retention should be culturally appropriate, voluntary and should leave the right of the adolescent and family to opt-out.^[2,9,10]

CONCLUSION

This illustrative manuscript shows a systematic study of the long-term relationship between the exposure of VR/AR and axial length of the eye of adolescents in Mosul using IOLMaster 700. The results obtained illustrate the consequences of increased exposure, which can be seen to be associated with increased axial elongation, increased negative refractive change and increased visual symptoms.

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