IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)
An International Open Access, Peer-reviewed, Refereed Journal

FACING THE CHALLENGES OF MYOPIA DURING QUARANTINE: AN UPDATE

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Abstract: The aim of this review is to elucidate the mechanism and the factors responsible for myopia boom and the management options during quarantine and prolonged lockdown period due to COVID pandemic. Understanding the pathogenesis and factor accentuating the progression of myopia under present circumstances may help clinicians to modify current care system that is likely to reduce the morbidity associated with the refractive error. The rapid increase in the myopia could be the result of the interplay between genetic and the present environmental factors. The review revealed the critical measures needed to be implemented to control myopia keeping in mind the restrictions required for preventing the further spreading of the pandemic.

***Index Terms* – Myopia, Pandemic, COVID-19, Progression.**

I. INTRODUCTION

COVID-19 pandemic has changed the priorities of life, almost overnight, from real world interactions to the online space. The optometrists in India have started addressing the far-reaching consequences of the enhanced screen time and less outdoor time – that is likely to harm vision in adolescent population and put them at higher risk of developing myopia. Myopia is a common ocular disorder, with around 2.5 billion myopic people around the world [1]. The estimates of WHO that half of the population of the world may be myopic by 2050 shall be reached sooner if appropriate preventive measures are not taken [2]. Vision impairment related to myopia not only has a significant economic impact but adversely affects the quality of life with regard to patients' physical, emotional, and social functioning [3].

The rapidly increasing incidence of myopia along with the economic burdens caused during covid pandemic calls for assessment of the causal factors, possible treatments, and efforts at prevention. Although some insights have been made into molecular pathways underlying myopia [4] new drug targets [5] and drugs for treatment of myopia needs to be explored. Stopping the progression of myopia has the potential to positively affect quality of life and ocular health. The focus of this review is to understand the treatment options of myopes having restricted outdoor activity and are forced into more screen time during quarantine and prolonged lockdown period due to Covid pandemic. This review also intends to explore new drug targets for the development of more effective treatment options in future for myopia.

II. PATHOGENESIS

Myopic syndromes have mild to severe clinical manifestations and is a progressive eye disease with potentially dangerous impact on daily lives. While the prevalence of myopia has been reported to be very high in East Asia it was not a cause for major concern in suburban India. However, urban population in India had been witnessing progressive increase in the prevalence of myopia even during pre-covid era [6]. Detailed studies on prevalence of myopia is needed in the post - covid scenario as majority of children are forced to stay indoors and are having prolonged screen time.

Experimental studies with animal model (Chick guinea pig monkey and zebrafish) have been guiding our knowledge on ocular growth and potential mechanism leading to myopia. These studies revealed that the eye growth is visually controlled by retina and emmetropization uses sophisticated cues and does not depend on its connection to brain [7]. During postnatal eye growth, the precise matching of the axial length (the distance from the anterior corneal surface to the retina along the visual axis) and the optical power of the eye brings the eye to emmetropia [8]. Variation in axial length and refractive power of cornea and crystalline lens with respect to axial length of eye contribute to the refractive errors [9].

Retinal defocus results in signaling cascade in retinal pigment epithelial (RPE) cells, choroid and sclera leading to further alteration in overall growth and creation of refractive errors [10]. RPE relays the retinal derived growth modulatory signals to choroid and sclera that in turn controls the vitreous chamber depth and eye length [11]. As RPE and choroid, have been linked to altered eye growth, both of these tissues are potential targets for novel therapies for treatment of myopia [12]. Strong evidences support the important role of genetic factors in causing the pathogenesis of myopia [13]. Studies on RPE had revealed that bone morphogenetic proteins (BMPs) have

bidirectional regulation during ocular growth [14]. BMP2 was upregulated in induced hyperopia and down regulated in induced myopia [15] It needs to be mentioned here that BMPs are involved in the TGF-beta/BMPs pathway that regulates ocular growth [16]. Studies on the choroid indicated that there existed differences in gene expression in the choroid if compared between eyes with induced myopia and control ones [17]. Sclera also plays an important role in controlling ocular size and there is alteration of scleral gene expression during the development and recovery of induced myopia that tend to be consistent during the development and recovery of induced myopia. Prolyl 3-hydroxylation is a crucial posttranslational modification of collagens and prolyl 3-hydroxylase 2(P3h2) null animals had altered collagen prolyl 3-hydroxylation which can partly explain the cause of abnormalities in the structure of the sclera, during progressive myopia [18]. Mutations in the gene encoding P3H2 (LEPREL1) have been identified to associated with non syndromic severe myopia.
Animals studies have also supported theory that the environmental factors influence ocular growth regulation. Negative defocusing lenses, move the plane of focus behind the retina, and accelerated eye growth in young animals, thereby inducing myopia [19]. Human epidemiological studies have also provided convincing evidence for environmental influences, with near work and more indoor activities being among the factors identified to affect prevalence of myopia [20]. Quarantine measures for limiting the spread of global covid pandemic has decreased the time spend outdoors and youngsters relying more on near work, digital learning and on screen activities [21] Studies have suggested that there exits correlation between environmental factors and the pathological axial elongation of the eyes – a characteristic of myopia

II. Effects of Key Environmental Factors on Myopia

Some of the important environmental factors that can lead to myopia and associated problems during post - covid quarantine period are shown in Figure 1. They include:

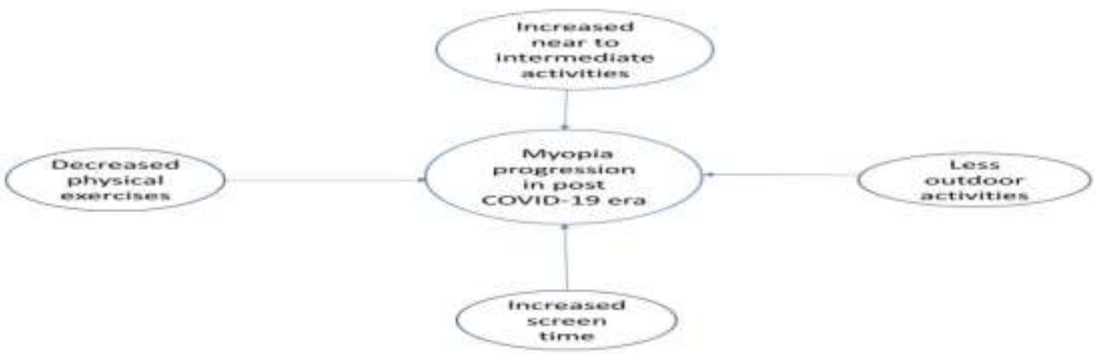

Figure 1: The schematic representation of factors causing Myopia during COVID-19 era

Near Work and Education
In school going children, myopia has long been found to be associated with increased levels of book reading and near work in dim light. Indeed, numerous studies conducted across a range of different populations have consistently found that higher levels of education are associated with a higher prevalence of myopia [22]. Continuous reading (>30 minutes) is also an important factor that contributed to myopia. This can be interpreted in the context of current theories of myopia as a close reading distance may provide a source of hyperopic defocus to the eye and, in conjunction with accommodative responses in susceptible individuals, could promote eye growth.
The higher prevalence of myopia has been reported in Asian children and can be often been attributed to the more intense schooling undertaken in Asian countries [23]. However, when studies were undertaken with similarities in near-work patterns for different Asians children suffered more from myopia as compared to European Caucasian children indicating that ethnicity may be independently a strong marker of risk for childhood myopia [24]. More such studies during post covid era can done to establish direct link between ethnicity and morbidity associated with myopia [25].
A higher prevalence of myopia exists in children living in urban regions, compared to children living in rural regions [26]. Studies have revealed higher myopia prevalence independent of conventional myopia risk factors such as ethnicity, parental myopia, the levels of near work, and outdoor activity for children living in city areas with higher population density [27]. These associations between the urban environment and myopia could at least be partly explained by socioeconomic and educational differences between urban and rural regions.

Screen Time
Increase in online learning and screen time has enhanced the time spend on near work during post covid era increasing the risk of myopia onset and progression in children. Studies have an association between increased computer use and myopia [28]. Use of the smartphone screen, has also been found associated with myopia [29]. However, association with television viewing and myopia has not been established. Some reports suggest that watching television induced a transient myopia that may lead to the development and progression of permanent myopia [30]. However, the viewing distance, duration were very important factors that needs detailed analysis. Reports suggest that watching television with recurrent short intermission at more than 2.8 meters of viewing distance did not affect the refractive error of children [31]. Detailed study and proper guideline in this area are needed to be generated immediately.

Light Exposure and intensity
A number of recent studies report that the time children spend engaged in outdoor activities is negatively associated with their risk of myopia [32]. Both cross-sectional and longitudinal studies indicate that greater time spent outdoors is associated with a significantly lower myopia prevalence and reduced risk of myopia onset in childhood [33]. Spending time outdoors for a period of at least >2 hours/day has been reported to down regulate the progression of myopia [34], however in post - covid scenario the outdoor activities in children have become highly restricted. This might have adverse impact on progression of the disease.
Reports suggest that the mechanisms through which outdoor light might protect against myopia, may include (a) stimulation of intensity- or wavelength-dependent anti-myopia systems in the retina, (b) sustained pupillary constriction via the melanopsin system – that may improve the retinal image quality by reducing longitudinal aberrations, (c) increase the production of vitamin D , (d) increase the viewing

of distant objects outdoors reduces accommodative fatigue, or (e) increase the activation of spatiotemporal image-response mechanisms in the retina, which might inhibit progression of myopia [35]. Norton et al. had reported that natural and high-intensity light prevent eye growth due to the dopamine release mechanism and promote emmetropization by cornea flattening [36]. It has been suggested that differences in set points in accommodation and emmetropization may result from the ratio of parasympathetic to sympathetic innervation [37]. Another possibility is the set point differences may result from the difference in color/luminance spatial and temporal contrast sensitivity, which determines the weight of the signals for myopic and hyperopic defocus [38]. Evidence from many experiments has revealed that color is important in producing accurate accommodation [39].

Animal studies have indicated that the intensity of daily light exposure can influence refractive development. In normal growing young chickens, rearing animals under a normal daily light-dark cycle, but with daily bright ambient lighting (~10,000 lux) resulted in significantly less myopic refractive errors than when animals were reared under dim ambient lighting during the day (50 lux) [40]. Bright light exposure also inhibits the development of FD myopia in a range of different animal species [41], with the strength of inhibitory effects correlating significantly with the log of the intensity of ambient light exposure [42]. Apart from accommodative errors, variability of the sensitivity of the emmetropization mechanism to color and luminance cues, and their relative sensitivity, are directly related to inaccuracy of the emmetropization response. Collectively, most of the studies carried out so far suggest that increased light exposure may associated with slower axial eye growth and may prevent rapid progression of myopia.

Nutrition

COVID-19 has become global public health nightmare as lockdowns led to diet and lifestyle changes. Studies have suggested that there have been low levels of physical activity and perceived weight gained during the lockdown period [43]. School environment provide structure and routine around meal times that provide protection against obesity. Closure of school during Covid -19 pandemic is likely to have collateral effect on body weight of children as they had less chance for continuing exercise [44]. BMI has been associated with an increased prevalence of myopia. Scientists have shown that heavier individuals have tendency of becoming hyperopic [45]. Reports suggest that accumulation of retro-bulbar fat prevents expansion by limiting the orbital space [46]. Making obese individuals to be more hyperopic vision with shorter vitreous chambers [47]. However, confusion still exist as some workers did not find clear relationship between myopic refractive error and weight or BMI [48]. Government of countries around the globe are not only dealing with the burden of the COVID-19 and its enormous strains on the health care system, they are also battling a destabilization in their economies and a rising threat of food insecurity in a section of population [49]. Earlier studies had revealed that the children who developed myopia had a generally lower intake of many of the food components (protein, fat, vitamins B1, B2 and C, phosphorus, iron, and cholesterol) [50]. Reports suggest that sunlight exposure, along with the vitamin riboflavin strengthens the structure of the sclera making it less prone to the stretching associated with axial elongation leading to myopia [51]. However, there are no studies to directly demonstrate that Vitamin D making sclera strong enough that resist the stretching associated with progressive myopia. Nutrients responsible for structural proteins like collagen include calcium, magnesium, silica, selenium, manganese vitamin C and bioflavonoids [52]. However, we lack the data to support the suggestion that additional intake of these nutrients may strengthen the collagen matrix and decrease the risk of scleral stretching. Reports suggest that Vitamin E has been used in the treatment of progressive myopia [53]. However detailed analysis of nutrition on myopia needs to be ascertained in post COVID era.

III. MYOPIA MANAGEMENT: CONVENTIONAL TECHNIQUES WITH LATEST TECHNOLOGY

Currently, there is no specific studies on most appropriate management option to prevent myopia progression. However, many factors like the patient's age, rate of myopia progression and amount of refractive error needs to be taken into consideration while choosing the management option [54]. There are various advancements coming up in the otherwise conventional management methods.

Spectacles

Some recent promising spectacle lens designs like the Defocus Incorporated Multiple Segments (DIMS) lens, developed in Hong Kong and only available in Asia (Myo Smart, Hoya), is shown to reduce myopia progression by around 50% [55]. Additionally, SightGlass Vision, based in California, recently announced promising interim results from a randomized clinical trial of their spectacle lens design and have also presented positive data on patient tolerability [56].

Soft Contact lenses

Soft contact lenses are increasingly used as a myopia management option, with solid scientific evidence to support their use. Center distance multifocal soft lenses, which were originally intended for the correction of presbyopia, are shown to have a positive effect on myopia progression when fit on young myopes [57]. However, there are lenses specifically designed for myopia control (Dual focus lenses and extended-depth-of-focus lenses) both have been shown to slow myopia progression [58].

Orthokeratology

In association with 50 years old orthokeratology (ortho-k) method to correct myopia, introduction of reverse geometry lens designs and high permeability materials have become a very popular myopia control management option with 30% to 80% slowing of axial elongation [59].

Combination therapies

It would be reasonable to assume that if myopia control is modulated by different mechanisms combining treatments may be more effective than a single method. The obvious option would be to combine atropine with either ortho-k or multifocal soft lenses [60]. Currently, there is insufficient evidence in the literature to recommend this as a first-line treatment option, but such an approach could be valuable in patients who continue to experience rapid progression using a single treatment.

In spite of various studies showing positive responses in controlling myopia progression [61], above mentioned options can be practiced rarely due to present pandemic scenario as these methods demand vigorous clinical assessments and panic driven people are afraid of going to any clinic or hospitals. Table 1 reveals the need for modifying the ophthalmic practices in post covid scenario so that the safety of clinicians and patients are maintained.

Ophthalmic Practice	Pre-COVID Phase	Post-COVID Phase
Screening of patients and co-workers even if they are asymptomatic	N/A	-Use of non contact infrared thermometers -Symptom assessments like: coughing/shortness of breath, red eye
Cleaning of equipment after every check-up	N/A	A must process especially with disinfectants
Use of breath shields/Barriers for slit lamp	N/A	Highly recommended
Use of disposable equipment	N/A	As much as possible
Hand wash	Only before CL (Contact Lens) trial and after any contagious case	Before and after handling each patient, before eating and after using washroom
Use of a single phone or computer and social and physical distancing between staffs	N/A	-Should be strictly maintained -Need to disinfect between uses if required
Tele-medicine/Tele-optometry	Restricted to remote practice	Need of the hour to avoid cross contamination
Utilization of PPE (Personal Protective Equipment)	N/A	Need of the hour to avoid cross contamination
Cleaning of examination room in between each patient visit with disinfectants	N/A	Highly recommended

Table 1:- The modifications in ophthalmic Practice in Pre and Post COVID-19 era

IV. MYOPIA MANAGEMENT IN THE LIGHT OF COVID-19 PANDEMIC

In the setting of community spread of COVID-19, treating myopic patients safely is a challenge. In-office myopia management visits may not be possible or as frequent these days. Thus, it is vital to communicate effectively with patients outside the clinical set up so that they understand the importance of, and adhere to, their specific myopia management plan. This can be accomplished through telemedicine visits as well as communicating through digital systems [62]. The consequences of high myopia are well understood, and multiple evidence-based treatment options exist to combat the development of high myopia. The challenge today is communicating these to patients and delivering the treatments. Table 2 depicts the challenges faced by clinicians which need to be addressed while controlling myopia progression.

Age Group	Challenges faced due to home quarantine
1-2 Years	-Less outdoor activity -More near and indoor work leading to use of more accommodation which can induce myopia and if left unnoticed can lead up to Amblyopia.[22,23]
3-18 Years	-Less outdoor activity -Increased exposure to digital screens due to the advent of online classes and education as part of COVID-19 regulations. -All these predisposes to the use of excess of accommodation stimulating the myopia progression.[28] -Apart from these an increased exposure to the digital screens in all lead to reduced tear production rate and less eye blinking rate which might trigger the manifestation of Dry Eye Disease (DED) in these individuals.[29]
Above 18 Years	-All the problems as it is discussed above. -Though myopia progress in this age group is still an area less cultivated but more or less the individuals will be exposed to the consequences to some extent.

Table 2:- Challenges as faced by practitioners (Age-wise distribution)

V. DISCUSSION

Myopia is a significant public health problem and its prevalence may be increasing over time. The pandemics has upset clinical practices followed in pre covid era during the forthcoming months or years. SARS-CoV-2 seems to be problem for clinicians—with a risk of infection through contact with eye secretions of patients—and for patients—with a delay in the management of the problems associated with myopia. COVID-19 pandemic has fostered development of skills that was not practised frequently in clinics earlier. Considering the contagiousness of the SARS-CoV-2, teleconferencing can be used as tools to avoid delays in attending to the patients. Personal protective equipment, gloves and filtering face piece respirators (FFP2 or FFP3 masks) for clinicians and surgical facemasks for the patient is necessary in daily clinical practice [63]. A Plexiglas barrier (protective shield) between patient and clinician is as additional approach during close clinical examinations.
The main treatment options that may slow the progression of the disease include spectacle lenses, contact lenses, and pharmaceutical agents. However, treatment with many of these options needs special care so that clinicians do not violate social distancing.

Therapeutic treatment does not violate the norms of social distancing however there are currently no pharmaceutical agents approved by the US FDA for use in treatment of myopia. More studies are needed in this direction.

A non-selective muscarinic antagonist, Atropine eye drops at low concentrations have been shown to slow myopia progression [64]. This treatment option may be considered in the present scenario in young myopes. The side effects of the drug in long term include photophobia and cycloplegia which are unacceptable to many clinicians. Use of another M1/M4 muscarinic antagonist Pirenzepine, has less side effects [65]. Clinical trials of pirenzepine had been promising but the clinicians do not prefer the drug because of its lower efficacy as compared to atropine and dosing included that the drops are administered twice a day as compared once a day regime of atropine drops. Two other ophthalmic antimuscarinic drugs, tropicamide and scopolamine, have also been reported to slow myopia progression [66]. However, treatments were not randomized and no follow-up studies were conducted.

Animal experiments had indicated that retinal dopamine are reduced in eye leading to the development of myopic eye [67]. Use of dopamine analogues for reducing the progression of myopia, needs detailed study in future.

Another candidate molecule was adenosine receptor antagonist, 7-methylxanthine (7MX). The results of animal study were promising. While 7MX oral therapy has several advantages for children, its effect on myopia progression was only very small [68]. However, this has opened up the possibility of conducting trials with adenosine receptor antagonist in post covid era.

Correction of peripheral ametropia/aberrations by specially designed contact lenses worn during the day or by orthokeratology with all caution may be done.

The options appear to be promising during post covid era include correction of peripheral ametropia/aberrations by increasing the outdoor activity, restoring to proper nutrition and reducing obesity while maintaining social distancing. In virtual education system a guideline providing a compulsory no-gadget intermission time is the need of the day. The maintenance of proper distance along with short intermission while watching television needs to be counselled by clinicians Maintaining visual hygiene which includes maintaining at least an arm working distance, preferably working with gadgets while having access to natural lights, reading under ambient illumination, using larger gadget screens for better resolution and reduced visual fatigue, ensuring frequent blinking to ensure that children do not develop dry eye disease-related symptoms. The font size on the digital device can be enlarged for increased visual comfort, as smaller font sizes are known to increase the cognitive demand. Text size of twice the individual's visual acuity is recommended for young, visually normal subjects for sustained comfort.

Thus we may conclude that lifestyle changes associated with covid pandemic (Figure1) exposed billions to the cumulative, well proven, risk factors for myopia which needs to be handled by clinicians with utmost care.

VI. Acknowledgment

The authors would like to acknowledge support received from Director, School of Health Sciences, NSHM Knowledge campus for conducting this review. The authors have no financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the article apart from those disclosed.

No writing assistance was utilized in the production of this article.

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