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## Xerophthalmia and Its Preventions through Different Strategies: A Review

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Xerophthalmia is a progressive disorder which results due to deficiency of vitamin A. It is a form of dry eye that can dry out your tears duct and eyes and it was recognized medically as far back as 1520BC. It can mainly result into night blindness which is a condition when person is unable to see in dim light which results due to low serum retinol levels in the body and it can cause serious damage to cornea which is the outer layer of our eyes and eye fail to produce tears. Vitamin A deficiency and Xerophthalmia particularly affect the children who are suffering from measles or malnutrition and it also affects pregnant women. Vitamin A deficiency can form white spots on our eyes and may cause ulcers on our cornea. It is one of the major eye disorders all over the globe and it results due to several factors such as poor dietary consumption of fruits and vegetables, smoking, poor socioeconomic status, poor absorption of vitamin A in the body, malnutrition in children and poor dietary habits. It is most common in children of 4-5 age group and it also causes morbidity and mortality among the children studying in school in many developing nations. It can be prevented by using administration of retinol rich foods, lifestyle management, healthy and nutritional dietary intake, proper counselling of patient, artificial tear administration, consumption of omega 3 fatty acids, carotenoid rich foods and vitamin A therapy.

**Keywords:** Vitamin A, xerophthalmia, night blindness, nutritional management

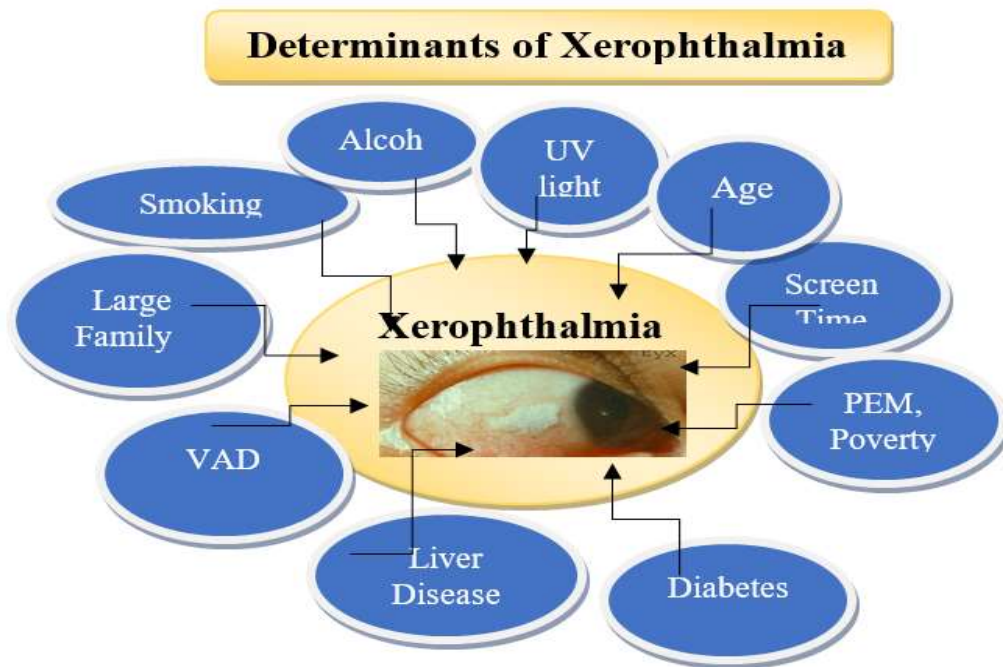
### INTRODUCTION

The word "xerophthalmia" states to the spectrum of optical appearances due to vitamin A deficiency. It is impaired sensitivity of the retina to light and epithelial disorders of the cornea and conjunctiva. Xerophthalmia encompassed conjunctival xerosis, Bitot spots, corneal xerosis and keratomalacia (WHO, 2014). The WHO has classified the clinical signs in xerophthalmia as the following: Night blindness (XN), Conjunctival xerosis (X1A), Bitot spots (X1B) Corneal xerosis (X2), Corneal ulceration/keratomalacia <math>\lt; \frac{1}{3}</math> corneal surface (X3A), Corneal ulceration/keratomalacia

$\geq \frac{1}{3}$  corneal surface (X3B), Corneal scar (XS) Xerophthalmic fundus (XF), Night Blindness (XN) Night blindness or malfunctioning visualization in presence of dim light is the primary medical sign to detect deficiency of vitamin A. It is also checked together a delicate and specific indication levels of serum retinol. Conjunctival Xerosis (X1A) is known as very dry and dull appearance of the conjunctiva membrane and it could be abnormal cytological impression of conjunctiva. Primary cause, is modifications in the protein's tissue of the epithelial tissue along the damage of goblet cells and inadequate mucous secretion make

contribution to this abnormality. Bitot's Spots (X1B) are pale, impermeable kind of pledges on the eyelid of conjunctiva, in the inner side of eyelid region. It is observed more commonly in the chronological conjunctiva. A Bitots spot is a group of keratinized and cause exuviation in epithelial cell and its symptoms shows as an inflamed area over the conjunctival portion. Corneal Xerosis (X2) is unclear and very dry kind of the corneal portion. It may start as epithelial lesions on the outer surface of cornea. This phase later rapidly progresses into soften and dryness of corneal cells, also known Keratomalacia. This stage is reversible to normal eyesight by the supplementation of high-dose of Vitamin A for the maintenance of vision. Corneal Ulceration and Keratomalacia (X3A and X3B) is described as transition entire cornea part into very weak and soft tissues and clinically it is called colliquative necrosis. Corneal Scar (XS) is damaging of tissues layer of cornea by the deficit Vitamin A in the body could be result of co-morbidities for example severe diarrhea, lack of protein-energy, or bronchial infection e.g., asthma or tuberculosis. Other secondary reasons must be checked. Xerophthalmic Fundus (XF) is the structural changes in the retina by the Vitamin A deficiency and leads to functional of retina and poor vision. (WHO, 1982). There are two causes of Xerophthalmia. Primary cause of vitamin A deficiency is deficiency of sufficient consumption of vitamin A and might be worsened by high proportions of infection, particularly diarrhea and measles. It is one of the utmost significant reasons of avertable childhood blindness and is a foremost contributor to morbidity and mortality from infections, specifically in children and pregnant women, affecting the deprived sectors of inhabitants, mainly those in low- and middle-income countries. (Akhtar et al., 2013). Moreover, a diet with long-lasting inadequate vitamin A will affect the growth emission of a child and worsen illness that can affect absorption appetite, transportation, and storage capacity. This greatly increases the risk of health significances (Menkir et al. 2008). It is observed that secondary cases of Xerophthalmia are not associated with intake of dietary Vitamin A. It is found infrequently in people but it could be the reason of malfunctioning liver e.g., storage and metabolic function and other metabolic disorders or chronic diseases which result in insufficient presence of vitamin A to function properly (Han et al. 2019). Vitamin A deficiency (VAD) is the third utmost communal nutritional deficiency in the domain, affecting

growth and vision in billions of children and pregnant women (Wassef et al., 2011). Vitamin A is essential in minor quantities by humans. As preformed vitamin A, it take place in several animal products (including liver, cod liver oil, butter, and egg yolks), and in selected fruits and vegetables (dark green leafy vegetables, carrots, mangoes, and papaya) it occurs as provitamin A carotenoids (including beta-carotene), which can then be converted to vitamin A in the intestine and other tissues (Semba, 2005). Vitamin A/all-trans retinol/atROL and its metabolites (retinoids) play acute roles in human functioning, containing eye development, maintenance of the optical system and photoreception (Von Lintig, 2012). Vitamin A is a pioneer photopigment in the retina, and play role to help the brain a in the visual classification. In the retina cells the rhodopsin system in the rod cells is much more susceptible by the Vitamin A deficiency than the method of iodopsin in the retinal cone cells. Primary malfunctioning in visualization in fade light or nyctalopia, is by the early weakening of rod cells function. For the maintenance and propagation of the epithelium of the conjunctiva and cornea, Vitamin A is very essential for this role. So, the deficiency results in corneal ulcers, Keratomalacia, conjunctival corneal xerosis and corneal scarring. Worldwide, vitamin A deficiency is a public health delinquent 122 countries; surrounded by this, 45 countries have moderate to severe child night blindness, and these include Iraq, Sri Lanka, India, and Southeast Asia with 3.93%, 1.6%, 1.56%, and 1.2%, respectively (WHO, 2005). In Ethiopia, the national prevalence of night blindness between children was 0.8% and the national prevalence of Bitots spot among children was 1.7% (Kang et al., 2015). The socioeconomic status of families, a antiquity of passing roundworms in stool, and diarrhea were significant precursor risk factors in vitamin A deficient preschool children. The certain long-term solution to inhibit this nutrition-related, preventable blindness lies in altering the nutritional behaviors of the rural Indian population through behavior change communication by nutritional supplementation, alimentary training, and nutritional therapy (Pal et al. 2008).The pervasiveness amount in diverse regions of Pakistan have been studied that total of 154 children 0-15 years of age were stated to have been suffering from xerophthalmia from North West Frontier Province of Pakistan. One hundred and twenty-three children (79%) were age 6 years and below.



**Figure 1: An illustration of various determinants of “Xerophthalmia”**

Ninety-four children (61%) had blinding xerophthalmia (corneal xerosis, corneal ulcer, keratomalacia). Out of 94 children with blinding xerophthalmia, 73 (78%) of children were less than 3 years of age. Ninety-nine children (64%) were male and 55 children (36%) were female (Fatima et al. 2018).

#### **Determinants of Xerophthalmia:**

Xerophthalmia is considered one of the major eye ailments around the globe which is revealed on the first examination. The important determinants identified for xerophthalmia are related to lifestyle that play a pivotal role like poverty, poor eating habits, low intake of fruits and vegetables, too much screen time, alcohol consumption, diabetes, liver disease and many others. So, it is considered as problem which is related to public health (Sayin et al. 2014). These determinants can be categorized as nutritional as well as demographic and lifestyle factors. The dietary determinants leading to the vitamin A deficiency are poor eating habits, inadequate intake of food, low quality of vitamin A containing foods and breastfeeding age. Demographic factors include socioeconomic status of family, mother's education and nutritional status

(Paranjpe et al. 2019). The increased prevalence of xerophthalmia in women during child-bearing age and in neonates indicate the worth of adequate nutrients intake during rapid growth time. Older children are also suffer from xerophthalmia. The feeding practices of infants are highly associated with the subsequent risk of this eye disease which is negatively correlated with vitamin A rich food intake (Sherwin et al. 2012).

#### **Pre-school Children:**

The age 3-5 years come under the pre-school duration. It is very critical life period of child when he/ she enjoys liberty and independence. To support a child's mental and physical growth and development directly influence the child's development in pre-school years. Hence the closed monitoring of child's growth and development is very important in pediatric practices as children can be influenced by every situation which interferes (disturbs) the cognitive and physical health of children (Abdel-Wahab et al. 2016). Xerophthalmia is a major etiology of blindness during childhood. It may develop in any age group but the incidence of xerophthalmia is identified as highest in pre-school children.

Previously, it was considered that about 127 million children in pre-school age are deficient in vitamin A all over the world (serum retinol <0.7 mol/Liter) and 4.4 million children from which are suffering from xerophthalmia. Almost 33% of world's children in preschool age have sub-clinical vitamin A deficiency and 0.9 % have night blindness (Tariku et al. 2016). As the need for vitamin A are very high for the pre-school children due to their increased cognitive and physical growth and usually, they have low food intake due to this reason pre-school children are more vulnerable to the vitamin A deficiency. Moreover, frequent illnesses due to infections of respiratory tract (RTI's) and measles that result in depletion of vitamin A stores in the body, are very usual in pre-school children (Chiu et al. 2016). The deficiency of vitamin A may cause xerophthalmia and result in blindness retard growth, compromised innate and acquired immunity increased chances of infection and death. Although, the diet related chronic deficiency of vitamin A or vitamin A malabsorption are the main etiology of this vitamin's deficiency but it is highly associated or linked with several important determinants (Dole et al. 2009).

#### **Lifestyle factors**

A large number of evidences has revealed that inadequately varied diets, big family size, size, way of living, poor eating habits, poverty, droughts, processed food consumption, smoking and residing in an endemic prevailing locality, smoking, T.V watching, computer use specific disease condition etc. and improper hygiene, practices are the positive determinants of xerophthalmia (WHO, 2014).

#### **Food consumption**

The low intake of green leafy vegetables, yellow-colored fruits, carrots, or egg during weaning comparable to current consumption and age may increase the chances of xerophthalmia. The elimination of these foods (except for mango and papaya in older children) from the ongoing diet was correlated to 2-9 folds increased chances of xerophthalmia, adapted for weaning influences (Dole et al. 2009). The children who had no intake of vegetables and fruit for the minimum duration of one month were 3.18 times more prone to suffer from xerophthalmia when compare to those children having sufficient intake of fruits and vegetables (Belete et al. 2019).

#### **UV rays:**

The photochemical injury to eye may be caused by enormous and frequent exposure to ultraviolet radiation (specifically for UVB). Free radicals can be generated due to UV rays which inactivates or slows down the activity of antioxidant enzyme in the cornea of eye. The cornea absorbs UV rays and these rays may cause corneal injury, keratinocyte hyperplasia, disorders ocular surface, conjunctival connective tissue proliferation and can increase the eye's aging process and tissue around the eye. The continuous UVB's exposure may also result in pain and foreign body sensation in the eye, desquamated, degenerative cornea, inflammation of cornea lead to lower production of tears increased susceptibility of xerophthalmia (Lin et al. 2018).

#### **Protein energy malnutrition (PEM):**

Severe protein energy malnutrition is directly linked with xerophthalmia in children because nutritional imbalance can increase the risk of xerophthalmia particularly among those suffering from kwashiorkor (48.6-54.9%), leads to destruction of the cornea and blindness. Also delay or transient the corneal healing in children with PEM (Sen, 2020).

#### **Cash crop production and Maternal education:**

Poor intake of vitamin A containing foods is the main cause of xerophthalmia. There are many other reasons that are related to poor nutritional practices as family factors like low socioeconomic status or combine housing influence some children of a same age and gender to eat food inspired from other choices. Also, ignorance and prevalence of diarrhea, presence of infectious diseases as measles, hot, dry season and exposure to dust and smoke might be determinants of xerophthalmia (Wodaye et al. 2016). The production of cash crop and maternal education are two primary issues linked with xerophthalmia. Therefore, awareness given to community is must require to describe the importance of consumption of food rich in vitamin A to prevent vitamin A deficiency is highly suggested. Health educational program should be developed and implemented for mothers had children with xerophthalmia to provide them with the most recent information and proper practices toward care of their children. Booklets should be available and distributed to all mothers about the disease and health-related practices. Further studies need to be focusing on the associations

between proper nutrition and health (Abdulmalek and Benkhaial, 2018).

**Smoking:**

Active smoking is a known determinant of dry eye among adults while passive smoking is also a significant risk factor of eye infection and dryness of cornea in children. It can cause many chronic diseases which are still unclear risk factor of dry eye. A large number of literature studies described the worse effect of smoking on dry eye, which shows that smoking is the leading risk of dry eyes (Khokhar et al. 2016).

**Big Family Size:**

Large family size of children is more prone to suffer from night blindness also reduce their share of energy, protein, iron, and vitamin A causing the condition more worse. The prevalence of xerophthalmia was found in lower socioeconomic strata with a large family. Similarly, we also found incidence of xerophthalmia was more in lower middle class of socioeconomic group. Xerophthalmia was 3.9% in rural and 3.5% in urban areas (Agrawal and Agrawal, 2013).

**Low Socioeconomic Status:**

Many interrelated socioeconomic factors influence night blindness. The main reasons for declining levels of food intake is connected mostly to the greater living costs and increased rates inflation (Neves et al. 2019). The age allergic conjunctivitis blepharitis, ametropia and passive smoking are the risk factors of children's dry eye (Wang et al. 2020).

**Increased Screen Time:**

Young population are more vulnerable toward the video games and social media platforms. Modern people spend significant time using digital devices that worsen eye health, such as smart phones and computers (McLaughlin et al. 2014). As a result, the domestic rate of xerophthalmia has increased 75% (Gospe et al. 2016). Too much use of screen, increased risk of xerophthalmia, visual fatigue risks, obesity, insomnia, sedentary life style, depression, back pains, digital addiction, socialization and impaired academic performance are determined as adverse effects of video gaming and use of social media in youth (Alışkanlıkları 2020). In addition, 30% of those who use computers have experienced xerophthalmia. In other words, although most users are at risk of many eye

health deterioration issues accompanied by xerophthalmia, they may struggle to accurately recognize their own eye fatigue, and that they do not know how to manage their eye health has further fueled the health deterioration of the eye (Ko et al. 2016). As illness related to the eye is not easily recognized until serious, it is easy to neglect its management. However, regular eye care is essential to prevent xerophthalmia. When people have to focus on digital devices, particularly close range, it reduces the blink rate of the eye. This is the most significant factor that harms eye health. People using a lot of electronic equipment has continuously increased the incidence of eye diseases (Xu, Pu et al.2017).

**Alcohol Use:**

Alcoholic patients may have clinical disorders related to severe deficiency of some vitamins as retinol, due to a low consumption of healthy diet or malabsorption. Vitamin levels should examine in patients having symptoms related to their deficiency (Anita et al. 2019).

**Diabetes Mellitus:**

Type-2 diabetes is associated with xerophthalmia. Previous researches have described that diabetes is one of the main reasons of increased risks of xerophthalmia. Diabetes-induced xerophthalmia results glaucoma, cataracts, retinal degeneration and also a main cause of blindness. Diabetic patients suffer more from dryness of the eye, vision fluctuations, foreign body sensations and photophobia (DeMill et al. 2016). Proper monitoring of blood glucose level of diabetes patients and conducting ocular surface tests are helpful to avoid xerophthalmia. According to a study 70% and 57% of patients with type-2 and type-1 diabetes mellitus respectively suffer from dry eye syndrome (Kong, Yan et al. 2016). The function of tear film in diabetic patients could be affected by many factors including peripheral nervous diseases and poor control of blood glucose. It has also been shown that the quality of tear secretion in diabetic mice was significantly reduced, accompanied by atrophy of the lacrimal gland and weight loss of the tear gland (Yang et al. 2018). Type-2 diabetes mellitus distinguish certain association with xerophthalmia. Therefore, possible diseases of the ocular surface should considered when ophthalmologists execute routine checkup of diabetic patients, make it possible that timely and effective treatment can be prescribed (Wu et al. 2016). Either less production

of tear or more tear evaporation are due to photorefractive operations, type 2 diabetes, misuse of contact lens, juvenile arthritis, continuous use of eye drops, and atmospheric disruption by pollution. Systemic diseases in childhood like type 1 diabetes, primary and secondary Sjogren syndrome, connective tissue disorders, hypothyroidisms, juvenile arthritis, are main factors of xerophthalmia among children (Friedman et al. 2016).

#### **Nervous Disorder:**

Both rods and cones begin to become more sensitive to light as soon as a person steps into a dark place. While it takes less time to readapt to the day-light when a person comes out of the dark. Light adaptation is faster than night adaptation (Papalia et al. 2008). Night-blindness is to be attributed to interference with the functions of retinal rods, due to deficiency in visual purple. It may also appear as a functional nervous disorder associated with other symptoms of neurosis or malingering (Tandon, 2019).

#### **Down's Syndrome:**

Xerophthalmia is defined as a pathological condition in which the eye cannot produce tears resulting dryness of the tear film and successive ocular symptoms. Children with Down Syndrome have common eye infections, watering of eyes and blockage of tear drainage. The mild type of dry eye syndrome can be treated by simple treatments (Wladis, 2012).

#### **Liver Disease**

Liver have reservoirs of fat-soluble vitamin retinol (vitamin A) which is a crucial nutrient essential for sustaining immune function, eye health, growth, vision, and survival in human. Its deficiency can cause night blindness and xerophthalmia. Vitamin A deficiency, is more common in developing countries than developed world due to dietary inadequacy, liver disease especially cirrhosis (Tandon, 2019), while chronic malabsorption is the main etiological reason. Therefore people suffering chronic liver disease are at risk of xerophthalmia (Anita et al. 2019).

#### **Sjogren's Syndrome**

Improper functioning of the lacrimal glands (produce tears) results xerophthalmia occurs due to vitamin A deficiency that may result in a loss of mucus production by goblet cells leads to a compromised ocular surface and diminished wetting is associated with systemic disease

Sjogren's Syndrome (Cifuentes et al. 2018). It is a severe autoimmune disease occurred in the result of progressive and devastating inflammatory lymphocytic invasion of salivary and lacrimal exocrine glands with symptoms like parotid gland enlargement, xerostomia and xerophthalmia (Reed et al. 2018).

#### **Management of Xerophthalmia:**

##### **Patient Education Lifestyle Changes:**

Patient education should cover information on dietary modifications, protection from environmental pollution elimination of medications that aggravate illness. Practices that can reduce symptoms including good Personal hygiene. Chronic disease including Liver diseases and gastrointestinal diseases must be managed because these diseases are also major cause of Xerophthalmia. Use of humidifiers at home or in the workplace, avoiding smoking, reduced screen time is Environmental strategies to prevent Xerophthalmia. Persons who suffer from xerophthalmia must avoid exposure to smog and dust, pollen and other allergies and environmental polluting aspects. Weather condition like peoples who stay in a very hot environment also suffer from xerophthalmia. Eye drops and other eye moisturizers can help they add moisture that helps against tear loss (Buckley, 2018)

##### **Person Hygiene Practices:**

One of the most effective preventive measures is eyelid hygiene. Daily lid hygiene practices are suggested like cleansing products and gentle massage. Intervention studies showed that commercial warmed compresses on tear film stability were effective. Heated eyelid masks that are commercially available also helpful for patients. Increases in lipid layer thickness and tear breakup time were observed. All these products or treatments are an option to relieve xerophthalmia and dry eye symptoms (Jones et al. 2017).

##### **Reduction in Screen Time:**

Taking frequent breaks to rest the eyes during television viewing or reading, and maintaining hydration and reducing use of computer (Khokhar et al. 2016). Due to less blinking which in turn leads to rapid tear evaporation? Management included lowering the computer screen to below eye level that decreases the lid aperture and reduces eyestrain which is one of best effort to blink more often during reading or watching can help and improved the symptoms of

xerophthalmia (Alışkanlıkları, 2020).

#### **Artificial Tears Administration:**

Preservative free artificial tears are recommended they provide more relief and prevent from irritations. Restore tear film homeostasis is treatment goal. Administration of artificial tears and antibiotics in case of bacterial infection are Topical treatment. (Pan et al. 2017). Soft bandage lenses and medical approved contact lens are recommended because these lenses provide protection to greater area of the corneal surface. The physicians should educate and counsel the patient about eye care and how to prevent the eye dryness Maintains moisture. Wear sunglasses when going outdoors Patients should be encouraged (Froze and Kaufman, 2019).

#### **Corticosteroids and Xerophthalmia:**

Patients suffering from xerophthalmia and other dry eye disorders corticosteroids are effective disease modifying agents. Topical corticosteroids that increased intraocular pressure and the development of cataracts and others eye issue are not recommended for long-term. rimexolone, fluorometholone, prednisolone acetate and difluprednate these are example of Steroids which are useful for the treatment of xerophthalmia. Patients would be notified to read labels to check the ingredient list for tears and ointments to prevent use of products that causes dry eye disorders for example preservative benzalkonium chloride that exacerbates xerophthalmia (Cifuentes et al. 2018).

#### **Dietary Management of Xerophthalmia:**

##### **Role of Omega-3 Fatty acids:**

From the past studies evidence it shows that the increased intake of Omega-3 fatty acids will improve the tear production. Omega-3 have the anti-inflammatory properties that will help to improve the tear production and xerophthalmia that's why omega-3 is preferred on omega 6 and omega 9 fatty acids. There are many sources of omega-3 fatty acids that includes kale, broccoli, squash, whole grain and black kidney (McCusker, Durrani, Payette, & Suchecki, 2016).

##### **Role of Vitamin A and Carotenoids:**

Vitamin A is required for normal functioning of human eye especially maintaining for epithelial cellular integrity and visual system. Vitamin A has important role in visual system because Vitamin A

is a precursor of the photo pigment in retina. The lack of intake of vitamin A may cause Xerophthalmia in the developing countries those more effecting small children (Feroze and Kaufman, 2019). The normal intake of Vitamin A can help in normal immune competence, visual cycle, tissue differentiation and organogenesis. The inadequate intake Vitamin A can spread throughout the world and are responsible for blindness and unnecessary death each year. Beta-Carotene is important source of Vitamin A but are insufficient among the poor population (Sommer and Vyas, 2012).

#### **CONCLUSION**

Xerophthalmia is a major public health problem worldwide which occurs mostly due to chronic vitamin A deficiency, a third major nutritional deficiency of the world, or its malabsorption. It is more common in developing countries. The main vulnerable groups of xerophthalmia are pre-school children and pregnant women. In this review article, major nutritional, demographic, lifestyle, and disease related determinants have been elaborated. Early detection of such determinants is very crucial and must be focus of the prophylaxis programs for xerophthalmia. The susceptible children must be examined to evaluate vitamin A status. The health and nutrition education especially in mothers, are imperative to increase intake of fruits and vegetables to sustain and improve the vitamin A status in children and all age groups. The living conditions, hygienic practices and availability of vitamin A rich foods should be enhanced in vulnerable areas and communities. xerophthalmic patients should take proper medication along with diet therapy with focus on vitamin A, omega 3 containing foods and usage of sunscreen as treatment to control morbidity rate of xerophthalmia.

#### **CONFLICT OF INTEREST**

The authors declared that present study was performed in absence of any conflict of interest.

#### **AUTHOR CONTRIBUTIONS**

MBA: Conceptualization and methodology. MBA, IM, SN and RK: Writing original draft. AB, KJ and NS: Visualization and investigation. FZ and AC: Data validation. MBA, SN and IF: Writing reviewing and editing. All authors read and approved the final version. ORCID Sana Noreen <https://orcid.org/0000-0002-4040-5455>

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