

The correlation between keratoconus and eye rubbing: a review

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Received: 2018-10-24 Accepted: 2019-03-22

Abstract

• **Keratoconus is a non-inflammatory disorder which is gradual in development; corneal thinning and ectatic protrusion characterizes it. Keratoconus prevalence varies between different regions depending on several factors that affecting its prevalence. There are risk factors for developing keratoconus such as demographic and environmental factors. It was suggested that eye rubbing was associated with the development of keratoconus. The main aim of this review was to summarize the literature data about keratoconus and to identify the role of eye-rubbing in the aetiology of the disease. A number of 24 articles was reviewed through the PubMed, Google Scholar and Research Gates. There are many keywords used such as keratoconus, aetiology of keratoconus, eye rubbing, keratoconus prevalence, keratoconus and eye rubbing correlation. We concluded that eye rubbing causes the thinning of keratocyte, and the degree of effect of eye rubbing depends on the period and force of performing eye rubbing. It is recommended to avoid eye rubbing to prevent keratoconus, this can be achieved by avoiding itching and treating dryness of the eye and avoiding wearing eye lenses.**

• **KEYWORDS:** keratoconus; eye rubbing; keratoconus risk factors

DOI:10.18240/ijo.2019.11.17

Citation: Najmi H, Mobarki Y, Mania K, Altowairqi B, Basehi M, Mahfouz MS, Elmahdy M. The correlation between keratoconus and eye rubbing: a review. *Int J Ophthalmol* 2019;12(11):1775-1781

INTRODUCTION

Eye diseases are considered a critical health problem in the Middle East, especially in Saudi Arabia^[1]. Keratoconus is an eye disease causes curvature of cornea gradually, transforming it from a symmetrical dome shape into an asymmetric cone shape. This results in reduced visual acuity and a change in eyeglasses^[1]. It was described by Nottingham firstly in 1854^[2], this disease is accompanied by blurred vision secondary to irregular astigmatism^[2].

It affects all ethnic groups. However, it is more prevalent in Caucasians and Asians^[3]. The prevalence of keratoconus varies between different studies due to the differences in diagnostic tests as well as the definition of keratoconus; the prevalence was reported to be 1 case in every 2000 individuals globally^[4]. In Saudi Arabia, it was found that keratoconus in the previous 20y was the primary reason for corneal transplantation^[5]. Several factors increase the development of keratoconus including demographic factors and environmental factors, the demographic factors including ethnic differences and genetic factors, while ecological factors including eye rubbing, atopy and ultraviolet (UV) exposure^[6]. Postulation of keratoconus development by eye rubbing discussed multiple published case reports such as^[7] that suggest the association between keratoconus and eye rubbing. Eye rubbing is a common activity of the individuals that occurs in response to emotional stress, fatigue or ocular irritation, it happens also before sleep and when waking^[8]. Eye rubbing can be evoked by symptoms of allergy and dryness of eye^[9-10]. The current review aims to find out the association between keratoconus and eye rubbing by reviewing the previous studies and to summarize the literature data about keratoconus.

In this review, we have used the internet as a method to review articles discussing the current subject. The PubMed, Google Scholar and Research Gates are visited to have access to the selected articles. There are many keywords used such as keratoconus, aetiology of keratoconus, eye rubbing, keratoconus prevalence, keratoconus and eye rubbing

correlation; we obtained 24 articles, we excluded 13 articles as they did not meet the study criteria. Eleven articles only are included as they meet the study criteria; 3 of them were review articles, and 8 were original articles. The articles included in this review were published in the English language between 2003 and 2017. The information extracted from the selected articles included a definition of keratoconus, its pathology, prevalence, classification, symptoms, diagnosis, risk factors, and management.

KERATOCONUS

Keratoconus Definition Keratoconus is a term derived from the Greek word *keras* (horn) and *konos* (cone)^[6] which means cone-like protrusion of the cornea^[11]. Keratoconus is an eye disease causes curvature of cornea gradually, transforming it from a symmetrical dome shape into an asymmetric cone shape. This results in reduced visual acuity and a change in eyeglasses^[1]. This disorder has been known in the middle of the 19th century^[6]. Keratoconus is a non-inflammatory disorder that leads to thinning of the cornea, it usually occurs bilaterally^[12], in 96% of cases^[13], but it can develop asymmetrically^[14]. The vast majority of cases have bilateral keratoconus, but they are asymmetric in severity and progression^[6].

Keratoconus Pathology The disease may begin as unilateral, but finally, the other eye becomes involved^[15]. All cornea layers are affected by keratoconus, but corneal stroma is the most notable^[6]. Thinning of corneal stroma occurs at the inferior or central portion of the cornea, and it becomes thinner and causes distortion of the cornea resulting in a cone shape of the cornea^[17-18], this in turn results in changes in refractive powers^[11]. The thinning of the superior part of the cornea is very rare^[19]. Keratoconus is an acquired ectasia which causes irregular, progressive, myopic astigmatism^[15]. Myopia and irregular astigmatism are induced by the thinning of the cornea which leads to mild or even marked visual impairment^[19]. Corneal oedema and decompensation result in corneal scarring which further decreases the visual acuity in the advanced cases^[20]. Keratoconus appears between 10 and 20 years of age^[13]. At puberty, keratoconus has its usual onset, and it develops in many cases until the third or fourth decade of life then it usually stops^[13].

Keratoconus Prevalence Keratoconus prevalence differs between different studies, the prevalence ranges from 1/500 to 1/2000 cases globally^[21]. Corneal topography devices were used in recent studies and prevalence was found to be higher^[22-23].

It was reported that in the general population the prevalence rates ranged from 8.8 to 229 cases/10⁵ per year^[24-25]. The prevalence in Russia was estimated to be 0.3/10⁵ while prevalence in the US and central India was reported to be 1 per 2000 and 2300/10⁵ respectively^[25-26].

In Tehran study from Iran, the keratoconus prevalence was 3.3%^[27]. A review from Saudi Arabia mentioned the prevalence in several countries; it was stated that the prevalence in Columbia was 3900/10⁵, in Yemen was 15 500/10⁵ and 9400/10⁵^[11]. Keratoconus prevalence in Macedonia was estimated to be 6.8 cases/10⁵^[13] and in Israel was 2340/10⁵^[28]. A study from King Khaled Eye Specialist Hospital in Riyadh, Saudi Arabia, showed that the prevalence of keratoconus represented 0.81/10⁵ citizens. However, the authors suggested that these results may not represent the prevalence in Saudi Arabia assuming that patients may be referred to other ophthalmic facilities or hospitals^[1].

The prevalence of keratoconus in Asir Province, Saudi Arabia by using a clinic-based protocol was found as 20 cases/10⁵^[29]. Another study from King Khalid Hospital in Hail city, Saudi Arabia, showed that the prevalence between general population was 4/10⁵^[30] which was lower than the prevalence reported from Asir^[29]. The variation in prevalence rates between different regions in the world returns to change in different factors between various studies such as methods of assessment and diagnostic criteria^[11].

Classification of Keratoconus Keratoconus is categorized into three broad categories. The first involves keratoconus associated with rare genetic disorders (such as neurofibromatosis, Down syndrome and nail-patella syndrome). The second involves keratoconus associated with some factors such as eye rubbing, atopy, contact lens wear, Leber congenital amaurosis, mitral valve prolapse and positive family history, the third and last category involves keratoconus with no association and of unknown aetiology^[21].

Signs and Symptoms of Keratoconus Signs and symptoms of keratoconus differ according to the severity of the disease^[1]. In the early stages of the disease, the patients may experience no symptoms^[6], however they may experience some symptoms which involve increased sensitivity to light, seeing lights or haloes around objects, eye strain, irritation, allergy, pain, desire for rubbing, decreased resolution at all distances and blurred vision^[11,31]. The symptoms range from mild to severe visual impairment as a result of myopia, irregular astigmatism, and frequently, corneal scarring^[6].

There are three signs of keratoconus including thinning of the stromal cornea with subsequent ectasia, Fleischer's ring which reflects the deposition of iron (hemosiderin pigment) in the basal layer of the corneal epithelium and the breaks in Descemet's and Bowman's layers^[4,18].

Vogt's striae and Fleischer's ring are vertical lines produced by compression of Descemet's membrane which may be observed near the apex of the cone. The ectatic cornea becomes visible at the advanced stage of keratoconus; the protrusion pushes the lower lid out in a V-shaped dent by looking downward, this

called Munson's sign. In the most severe and advanced cases, breaks in Descemet's membrane takes place, and it referred to as hydrops have been observed. Stromal oedema and vision loss with associated pain results from these breaks^[32-33].

Diagnosis of Keratoconus Diagnosis of keratoconus regarding symptoms in early and mild stages is difficult as the first symptoms of keratoconus similar to that of other ocular conditions^[11]. The classic way to assess keratoconus involves external examination of the eye using both anterior segment expert opinion and utilization of same widely used scales^[11]. Keratoconus diagnosis became easier as a result of advances in corneal imaging^[12]. Electronic and molecular methods including elevation-based slit scanning and topographic are available now and increased dramatically as an essential tool for differential diagnosis and categorization of keratoconus^[11]. Retinoscopy can show irregular astigmatism as the disease progress. However corneal topography is the most sensitive strategy to detect early keratoconus^[6]. Corneal topography and tomography assessment instruments can efficiently use to diagnose keratoconus and to determine its level of severity; these strategies enabled performing of fine screening of the central corneal steeping, asymmetry of the interior corneal steeping and asymmetry of optical power^[11]. Ultrasonic pachymetry can show the difference between the superior and inferior thickness of the cornea, hence keratoconus grading can be done^[34].

The corneal topography has become a routine ophthalmic practice, it is considered now as the standard gold test in both monitoring and diagnosing of keratoconus^[4,18]. The pattern of the cornea on the topographic differs between keratoconus and normal cornea qualitatively and quantitatively^[6], the cornea appears as an asymmetric bow-tie with a skewed radial axis in case of keratoconus when diagnosing it qualitatively^[4]. In the quantitative evaluation of keratoconus, the area of corneal power increased, and inferior-superior (IS) power appears asymmetry^[35-36]. There were several video-keratography derived indices have been developed to assess the topographic pattern of keratoconus quantitatively^[6]. Posterior corneal surface elevation has an important role as a non-invasive method of diagnosis. It helps in measuring the extent of the injury, as well as it represents a very sensitive method of diagnosis^[37].

Causes and Factors of Keratoconus Risk The risk factors of keratoconus include demographic factors, ethnic differences, genetic factors and environmental factors. The ecological factors involve eye rubbing, atopy and UV exposure^[6]. Environmental and genetic factors are considered one of the possible causes, some genetic defects that cause keratoconus^[6], but there may still be many flaws to be discovered. In some cases, conical cornea appears in a number of family members,

especially in families where kinship occurs^[21]. Where scientists were able to identify a chromosome link has a role in this case. Keratoconus may be associated with other allergic diseases such as hay, eczema, asthma, this condition may be clearly related to the problem of eye rubbing, which may cause a rapid exacerbation. It may also affect people who use contact lenses^[11].

In the current review, we will highlight on eye rubbing as a risk factor for keratoconus.

EYE RUBBING

Definition and Causes of Eye Rubbing Eye rubbing is a common habit that occurs spontaneously before sleep when awakening and throughout the day as a response to ocular irritation fatigue and emotional stress^[8]. It was stated that abnormal eye rubbing could be secondary to bothersome symptoms such as dryness and itching, and it can be psychogenic with compulsive or unprovoked rubbing^[12]. Atopy and allergy were the most dominant risk factors for the chronic habit of abnormal eye rubbing^[38]. Also, compulsive behaviour, mental stress or emotional tension and psychogenesis are associated with abnormal eye rubbing^[39].

Eye Rubbing as a Risk Factor for Keratoconus Chronic abnormal eye rubbing is associated with keratoconus development^[6]. Repetitive gentle and vigorous knuckle-grinding rubbing are associated with progression of keratoconus^[40]. There are many reasons for eye rubbing habit. However, the reason will not affect the role of persistent eye rubbing in the development of keratoconus^[12]. Bilateral keratoconus was reported in a girl with four years old who practised persistent eye rubbing for long-term^[41].

In a survey that included 240 keratoconus patients, it was found that 65.6% of them had a history of eye rubbing^[42]. McGhee *et al*^[43] found that 48% of keratoconus patients rubbed their eyes. In the Saudi study, it was found that 44.8% of patients had eye rubbing^[30]. Rabinowitz^[44] in his case-control study reported that in 218 keratoconus patients and 183 healthy age-matched controls, eye rubbing was present in 83% of keratoconus subjects compared to 58% in healthy controls. A study from Iran showed that there was a healthy relationship between the positive history of eye rubbing and prevalence of keratoconus^[31].

In Saudi study^[30] it was reported that the most common risk factors between keratoconus patients were eye-rubbing representing 100%. Positive history of eye rubbing represented a higher frequency of keratoconus patients^[45]. Corneal curvature becomes worse by the asymmetric eye rubbing^[46]. Asymmetric keratoconus was found to be related to the eye that severely affected by abnormal eye rubbing^[47]. Monocular keratoconus in a patient with bilateral eye-rubbing was found to be related to hand dominance^[48]. Keratoconus develops

Table 1 Some articles outcomes in details

Authors	Type of study	Year of publication	No. of patients	Conclusion
Hashemi H, <i>et al</i> ^[27]	Cross-sectional	2013	263	This study provides the first population-based estimate of the prevalence of keratoconus in Iran. The prevalence of topographic keratoconus was high among citizens of Tehran districts 1 to 4. To confirm the hypothesis of a high rate of keratoconus in Iran, more extensive studies are needed which would examine the role of genetics and the environment.
Assiri AA, <i>et al</i> ^[29]	Clinical study	2005	125	44.8% of patients had eye rubbing.
Rabinowitz Y ^[44]	Case-control	2003	401	Eye rubbing was present in 83% of keratoconus subjects compared to 58% in standard controls. A study from Iran showed that there was a strong relationship between the positive history of eye rubbing and prevalence of keratoconus.
Gordon-Shaag A, <i>et al</i> ^[10]	Cross-sectional	2013	210	This study supports the hypothesis that consanguinity is a significant risk factor for keratoconus and provides strong support for a genetic contribution to the disease. Wearing sunglasses in this environment is beneficial, and the study confirmed that eye rubbing, allergy, and education are also significantly associated with keratoconus after adjusting for other predictors.
Alabdeltoneam M ^[1]	Retrospective	2012	1638	In total, 1638 patients were referred to King Khaled Eye Specialist Hospital for treatment of keratoconus from one of the five regions of Saudi Arabia at an average annual rate of referral of 136.5 patients per year. The overall distribution of keratoconus patients was almost equal between men and women, with a higher incidence in younger patients aged 16-26y.
Hassan H, <i>et al</i> ^[31]	Cross-sectional	2014	1280	Keratoconus may have a higher prevalence in the Middle East and Asia than in Western countries.
AlShammari Z, <i>et al</i> ^[30]	Retrospective	2016	About 12000 patients for each year	In this study, a significant relationship was found between increases in the age and the severity of the presenting features of keratoconus.

after 14mo in case of chronic compulsive eye rubbing and psychogenic eye rubbing^[12]. Also, it was found that eye rubbing was a significant risk factor in the development of keratoconus in patients with a history of parental consanguinity^[10].

Eye rubbing represented 91.8% of 49 children patients, where eye rubbing was secondary to induced ametropia or atopy^[49]. Other several studies failed to find an association between eye rubbing and keratoconus, as study from Lebanon reported no association between eye rubbing and keratoconus, where it showed that 12% of keratoconus patients had a family history of keratoconus, while eye rubbing was not a significant factor^[50]. In the other two studies by Owens and Gamble^[51] and Millodot *et al*^[52], it was found no significant association between keratoconus and eye rubbing (Table 1).

Mechanism of Keratoconus due to Eye Rubbing Several mechanisms have been suggested for the keratoconus development secondary to eye rubbing^[53]. The cornea is elastic and, therefore, susceptible to changes in shape. The frequency and force of rubbing are the factors that influence corneal eye rubbing related changes; these changes occur as the cornea is elastic, which made it susceptible to changes in shape^[12]. It was found that the keratocyte density in human corneas was reduced significantly by slight eye rubbing for 10s repeated 30 times over 30min^[54]. Also, changes in

intraocular pressure (IOP) due to eye rubbing can lead to the development of keratoconus, where indirect traumatization to keratocytes results from the significant fluctuations in IOP, this traumatization to keratocytes in turn results in keratoconus^[55]. Several studies^[56-58] reported that the level of IOP was found to increase by increasing the compressive rubbing forces that exerted in eye rubbing at the corneal surface.

Ocular Complication Result from Eye Rubbing Acute hydrops can be developed in patients with keratoconus of 9 years old of age as a result of continues eye rubbing^[59-61]. Hydrops in keratoconus patients may result from the mechanical stress of rubbing^[12]. Several studies showed an association between the development of acute hydrops and vigorous eye rubbing^[61-63]. Effects of eye rubbing on corneal topography were observed, where eye rubbing increase the irregularity index of the corneal surface, after 60s of eye rubbing, a 0.5 diopter of astigmatism was found to be induced^[53].

Management of Keratoconus The management of keratoconus differs according to the severity of the case, so there was no single method is the best for all patients^[64]. Spectacles can be used to correct mild keratoconus^[63]. Rigid contact lenses can be required then patient becomes unable to obtain good visual acuity as a result of higher order aberrations and increasing levels of irregular astigmatism, the rigid contact lens in this

case effectively provide a new anterior surface to the eye^[63]. There are several types of lens designs for keratoconus and it hard to predict which one is suitable for the patient, in addition, the corneal collagen cross-linking affects the frequency of keratoplasties in patients with keratoconus^[63].

Keratoplasty can be used as a separate management procedure for keratoconus, as it has different advantages upon long and short-term such as preserving the health of the host endothelium and preventing the rejection of the endothelial graft. In addition, as the graft survival is an important issue, it helps in the promotion of graft survival^[65].

CONCLUSION

Keratoconus is an eye disorder; its prevalence evaluation varies according to several factors. Several factors are affecting the development of keratoconus; eye-rubbing is the main factor which is causing a major number of eye injuries especially keratoconus. Eye rubbing causes the thinning of keratocyte, and the degree of effect of eye rubbing depends on the period and force of performing eye rubbing. Although few studies did not find a significant association between keratoconus and eye rubbing, the vast majority of the studies confirmed the correlation. It is recommended to avoid eye rubbing to prevent keratoconus; this can be achieved by the treatment or prevention of itching causes and treatment of dryness of the eye. In addition, it is recommended to avoid wearing eye lenses if they were unnecessary, also it is essential to increase awareness of individuals about the risk of eye rubbing as most of the persons are performing it as a habit.

ACKNOWLEDGEMENTS

The authors would like to thank all colleges and groups that helped in the production of this work in the University of Jazan, and specifically in the Faculty of Medicines and its different specialities.

Conflicts of Interest: Najmi H, None; Mobarki Y, None; Mania K, None; Altowairqi B, None; Basehi M, None; Mahfouz MS, None; Elmahdy M, None.

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