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KERATOCONUS IN ADULTS AND CHILDREN: EPIDEMIOLOGY, PATHOGENESIS, AND DIAGNOSIS

Djerad Noureddine*[a,b], Djerad Nadji[b], Boutrid Nada[c,d], Rahmoune Hakim[c,e]

[a] Ophthalmology clinic, El Eulma, Algeria.
[b] Ophthalmology Department, Ras El Oued Hospital, Algeria
[c] LIRSSEI Research Lab, Faculty of Medicine, University of Setif-1, Algeria
[d] Pediatrics Department, University Hospital of Setif, Algeria
[e] Pediatrics Department, EHS El Eulma, Algeria

[*] *Corresponding authors: Djerad Noureddine*
E-mail address: djerad.ophtalmologie@gmail.com
Tel.: 00213-541 41 74 87

Abstract

Keratoconus (KC) is a progressive, bilateral, non-inflammatory corneal disorder characterized by thinning and conical protrusion of the cornea, leading to significant visual impairment.
This minireview will focus exclusively on the epidemiology, pathogenesis, and diagnosis of keratoconus, providing an overview of the global prevalence and the various factors contributing to the disease's development. Notable geographical variations in KC prevalence are highlighted, with higher rates observed in certain regions, particularly in Asia and the Middle East. The pathophysiological mechanisms underlying KC, including mechanical stress from eye rubbing, genetic predispositions, and environmental influences such as UV exposure, are discussed. Additionally, the diagnostic approaches utilized for early detection and monitoring of KC progression are outlined.
By focusing on these foundational aspects, this minireview aims to enhance understanding and awareness of keratoconus as a vision-threatening condition.

Keywords : Keratoconus, epdiemiology, pathogenesis, diagnosis, children.

1. Introduction :

Keratoconus (KC) is a progressive, bilateral, non-inflammatory corneal disorder characterized by thinning and steepening of the cornea, leading to a conical shape, which is reflected in its name. It typically manifests during puberty and continues to progress until the third or fourth decade of life. Recent advancements in technology have enhanced our understanding of KC, revealing abnormalities in posterior corneal elevation and corneal thickness distribution [1,2]

2. Definition :

KC is an ectatic corneal disease characterized by progressive corneal thinning and protrusion into a conical shape. Spheroidal deformation results in profound visual impairment secondary to asymmetric astigmatism and myopia. Although it is bilateral, one eye is typically more severely affected than the other [1].
The etymology of the term KC comes from Greek words meaning “horn” (kéras) and “cone” (conus), where the conical shape of the cornea is described. As such, corneal thinning generally happens in the central or paracentral cornea and occurs most often in the inferotemporal region. Traditionally thought as a non-inflammatory condition, KC recently has been shown to be associated with substantial changes to inflammatory mediators in the KC eye [3].
KC occurs in all races and in both genders. It is usually an isolated ocular disease, but may be associated with other ocular or systemic diseases [1].

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3. Epidemiology :

Studies report notable global variation in KC epidemiology, and a recent meta-analysis involving over 50 million people from 15 countries found that the worldwide prevalence of KC is 138 cases per 100,000 individuals [4].
Interestingly, geographical variability is significant across regions and populations (Table 1). Surveys conducted in Asia, the Middle East, and Oceania have identified a higher prevalence, with rates ranging from 0.9% to 3.3% [5], with an astonishing study in Saudi Arabia that found 87.3 cases per 100,000 people among young adults [6].

Table 1 : Epidemiological Variations of KC Across Populations

Region	Particular Facts
Asia [5–8]	Increased prevalence in Middle-Eastern countries; genetic predisposition noted
Africa [5,9]	Limited data; higher prevalence among specific ethnic groups and high risk populations
Australia [5,10,11]	Environmental factors may play a role
North America [5,12]	Higher rates in certain regions; often diagnosed in late teens to early 20s
Europe [5,13]	Variability in prevalence; recent studies suggest higher rates in Mediterranean populations

There are also notable direpancies between adult and pediatric forms of KC, especially regrading the etiologies, the severity and the progression of KC.
Table 2 summarizes the differences between these 2 populations [14–16].

Table 2 : Characteristics of KC in Adult and in Pediatric Patients

Aspect	Adult KC	Pediatric KC
Onset	Typically begins in late teens to early 20s	Often diagnosed in childhood or early adolescence
Progression Rate	Generally slower progression	More rapid progression is common
Symptoms	Blurred vision, distortion, sensitivity to light	Similar symptoms but may include more severe visual impairment due to rapid changes
Diagnosis	Often diagnosed during routine eye exams or when symptoms develop	Diagnosis may occur earlier due to parental observation of visual issues
Treatment Options	Rigid gas permeable lenses, cross-linking, corneal transplant if severe	Contact lenses, cross-linking; surgical options considered earlier due to rapid progression
Prognosis	Generally favorable with appropriate management; slower progression allows for effective treatment	Variable; more aggressive management may be required due to rapid changes in corneal shape and vision

4. Pathogenesis :

Several key pathophysiological mechanisms and risk factors contribute to KC, summarized in 3 major points :

- Mechanical Stress: Frequent eye rubbing is considered a potential trigger for disease progression.
- Genetic Factors: Multiple genes associated with KC suggest a hereditary component.Changes in gene expression in epithelial and stromal tissue (MicroRNA Expression) have been linked to KC pathogenesis.
- Environmental Factors: eye rubbing, atopy (allergies, asthma, eczema) and UV exposure, as well as geographical factors

Eye rubbing is widely recognized as a risk factor for the development of KC : approximately half of KC patients report rubbing their eyes, although the percentage varies across studies. Significant differences are observed in the intensity and duration of eye rubbing: KC patients typically rub their eyes for longer durations (10 to 180 seconds) compared to individuals with allergic or infectious ocular conditions (<15 seconds) or those without any eye conditions (<5 seconds). Cases of asymmetric KC often show a correlation with more vigorous rubbing of the more affected eye : an 11-year-old boy developed unilateral KC after vigorously rubbing his left eye to relieve paroxysmal atrial tachycardia [1,3,17]. Case-control studies provide strong evidence supporting this association. A study by Bawazeer et al. demonstrated a significant link between eye rubbing

and KC, with an odds ratio of 3.98. However, some studies report high levels of eye rubbing in both KC patients and controls, particularly in dry, dusty climates, which may obscure the association [18].

Overexposure to ultraviolet (UV) light generates more reactive oxygen species (ROS), leading to oxidative stress and damage to the corneas of patients with KC, and this damage is linked to decreased levels of important antioxidant enzymes like aldehyde dehydrogenase class 3 (ALDH3) and superoxide dismutase, which are responsible for clearing ROS [19,20]. The observation that higher prevalence rates of KC occur in sunnier locales compared to Europe and North America supports this hypothesis; triggering weather conditions are common in Saudi Arabia, Lebanon, India, and Iran, unlike less sunny regions such as Finland or Japan [2,21]. Experimental evidence further supports this association: mice exposed to UV light showed stromal collagen degeneration, stromal thinning, and significant loss of keratocytes, and -similarly- UV exposure of anesthetized rabbit corneas led to cell apoptosis in all corneal layers [22,23].

Atopy has shown conflicting associations with KC. While many studies report a positive association, others find no statistically significant link due to methodological differences or variations in severity assessment. The aforementioned multivariate logistic regression analysis by Bawazeer et al. concluded that atopy is not directly associated with KC but is indirectly linked through induced eye rubbing [18]. Conversely, Kaya et al. found that KC patients with atopy exhibited a steeper and thinner ectatic cornea compared to those without atopy [24]. Asthma and eczema are less commonly reported than allergies, with lower prevalence noted in studies from regions such as the Middle East, India, and Singapore [4,5,18].

5. Clinical presentation :

KC typically presents with a range of visual and physical symptoms that can significantly impact a patient's quality of life. Patients often report blurred or distorted vision, primarily due to irregular astigmatism, and many others experience progressive myopia, which can lead to difficulty seeing clearly at both near and far distances. As the disease advances, patients may also notice increased sensitivity to light and glare, particularly at night, which can further impair visual function [1,3,25].

A thorough slit-lamp examination reveals characteristic signs of KC [1,3,25], including:

- Corneal Thinning: The cornea typically exhibits thinning, particularly in the central or paracentral regions, which is crucial for diagnosis.
- Conical Protrusion: The cornea may take on a conical shape, leading to a distinct appearance that is often identifiable during examination.
- Scarring: Scarring may develop as the condition progresses, particularly on the anterior surface of the cornea.
- Fleischer’s Ring: This brownish ring may appear at the base of the cone due to iron deposition.
- Vogt’s Striae: These are fine, stress lines seen in the corneal stroma that indicate mechanical stress and are commonly observed in KC patients.

In advanced stages, KC may present with additional clinical signs [1,3,25] :

- Munson’s Sign: This sign is characterized by an abnormal projection of the lower eyelid when the patient looks down, indicating significant corneal protrusion.
- Rizzuti’s Sign: A reflection seen on the corneal surface when light is directed from the side, indicating conical protrusion.

Severe cases can lead to significant vision loss, necessitating interventions such as corneal transplantation or other advanced management techniques. Patients experiencing acute complications such as corneal hydrops—a sudden swelling of

the cornea due to fluid accumulation—may present with severe pain, photophobia, and a marked decrease in visual acuity. Prompt recognition and treatment are critical to prevent further complications and preserve vision [17,26].
Several tools are used to confirm the diagnostic of KC [17] :
- Corneal Topography: This imaging technique is essential for diagnosing KC and assessing its severity : it provides detailed maps of the corneal surface, highlighting the irregularities that are characteristic of KC (Figure 1).

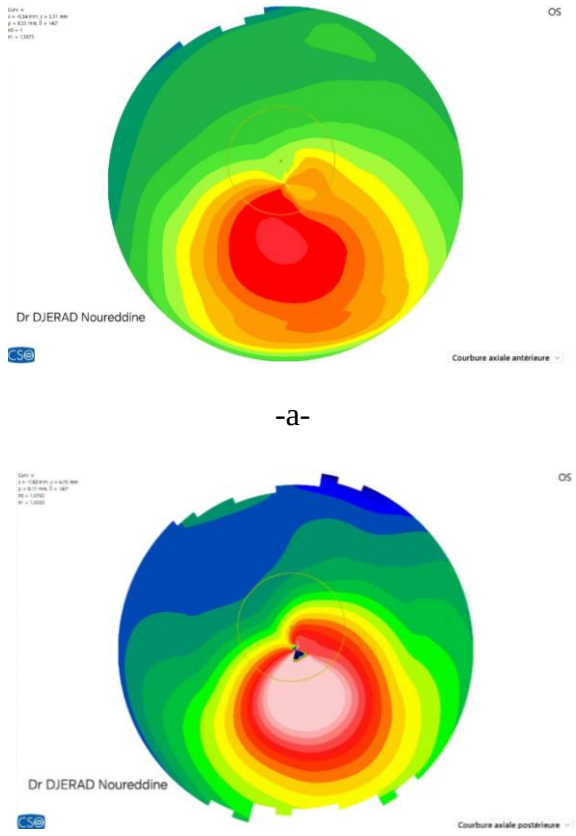

Figure 1 : **Corneal Topography of the Left Eye with Keratoconus in a 32 year Woman (Dr Noureddine Djerad personal data)**
a- Anterior Corneal Curvature
b- Posterior Corneal Curvature

- Tomography (Scheimpflug or Optical Coherence Tomography, OCT): These advanced imaging modalities are crucial for detecting early or subclinical stages of KC and subsequently monitoring the disease progression. They allow for a three-dimensional view of the cornea and can even reveal changes in thickness and curvature that may not be visible through standard examination methods.
Overall, early detection through comprehensive clinical evaluation and appropriate diagnostic tools is vital for effective management and treatment of KC.

6. Conclusion :

Keratoconus is a relatively prevalent condition that manifests differently across various geographic and demographic groups. Timely diagnosis through appropriate techniques is crucial for effective treatment. Implementing early detection through screening initiatives can greatly enhance management approaches for patients impacted by this vision-threatening disease.

Ongoing studies aim to advance knowledge about keratoconus pathogenesis and potential therapies that could improve patient outcomes or even reverse the condition.

Conflicts of interest : Authors have nothing to disclose

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