INTRODUCTION

The cornea represents a transparent avascular connective tissue that has a primary infection and structural barrier function. With the overlying tear film, it forms the anterior refractive surface of the eye optical system [1.]

Any disruption of the corneal fiber network can result in decreased structural integrity of the cornea, leading to decreased vision. One of the diseases that exhibit these pathological changes is keratoconus.

Keratoconus is a non-inflammatory bilateral progressive but asymmetrical disease. Described as corneal ectasia, thinning, gradual corneal protrusion and irregular astigmatism [2]. It usually starts during puberty with 75% of cases diagnosed before the age of 25 years [3].

Visual correction of early keratoconus may be achieved with spectacles and a large proportion of cases with advanced keratoconus may be correctable with rigid contact lenses. Surgical intervention is necessary when conservative management fails to achieve adequate visual rehabilitation. [4]

Corneal cross-linking has been described as the only modality in halting the disease progression over the past decade[5], by using Riboflavin eye drops and UVA light this

creates bonds between corneal collagen fibers in the stroma[6]. Cross-linking has been shown to generate various effects in the cornea such as increased stiffness, changes in biomechanical and bioelastic behavior of corneal collagen tissue and different visual, refractive, topographic and abberometric changes [7].

Wavelight Pentacam has helped us to detect early topometric, pachymetric and aberrometric changes, in subclinical and definite Keratoconus cases hence facilitating early diagnosis.

Aim of the Work

This study aims to investigate differences in objective and subjective out-come of collagen corneal crosslinking of different grads in keratoconic patients.

Chapter (1): Keratoconus

First described by german professor Burchard Mauchart in 1748 at the University of Tubingen, Germany. Keratoconus is a progressive non-inflammatory, degenerative disease that affects the integrity of the collagen matrix within the corneal stroma. Its hallmark is the formation of a localized cone-shaped ectasia; it is accompanied by thinning of the stroma in the area of the cone. This might cause irregular astigmatism and a steeper corneal curvature[6].

- **Etiology:**

Although it was described above that Keratoconus is a non-inflammatory disease, new studies believe that inflammatory mediators play a major role in its development[7]. An imbalance between degradative enzymes such as; lysosomal enzymes, cathepsins and matrix metalloproteinase-2 (MMP-2) and their inhibitors; Alpha-1 proteinase inhibitor, alpha-2 macroglobulin and tissue inhibitor of metalloproteinase-1 and 3 is now understood to be the reason behind the development of Keratoconus[8].

Atopy and rubbing the eyes are epidemiologically linked, a study reported that 48.2% of patients with keratoconus vigorously rubbed both eyes and only 2.2% rubbed significantly only one[9]. It was also found to be

associated with ocular diseases such as Leber's congenital amaurosis, granular corneal dystrophy, Avellino corneal dystrophy and posterior polymorphism dystrophy [10,11,12] and some systemic diseases such as Down syndrome, Ehlers-Danlos syndrome and osteogenesis imperfecta[13].

The disease was reported in identical twins and multigenerational families[14]. Prevalence of keratoconus is 3.34% in families with first degree relatives having the disease which is 15 to 67 times higher than the general population[15]. It is recently understood that KC has multiple genes responsible for its development.

- **Clinical Picture:**

- ***Symptoms:***

Clinically KC presents with unstable refraction usually consisting of myopia and astigmatism and variable visual acuity impairment however normal visual acuity may be present but only in early stages. Often the patient is symptom free until a relative advanced disease stage. It usually starts with:

- The patient complaining of decreased visual acuity at all distances, which cannot be compensated by correction, distortion of images.
- Photophobia.

- Glare and.
- Eye irritation making contact lenses uncomfortable are often characteristic symptoms of the disease grade.

- ***Signs:***

Some external signs of KC are worth mentioning;

- Munson's sign: which is the V-shaped protrusion of the lower eyelid by the lower cone when the patient is asked to look down, however this signis only apparent in moderate to severe cases while mild cases will not produce this sign since corneal bulging is minimal (**Figure 1**).

Figure (1): Munson's Sign[16]

- Rizutti's sign; consists of focusing a beam of light from the temporal direction of the cornea hence this will result in focusing the light on the nasal anterior sclera by the cone **(Figure** 2).

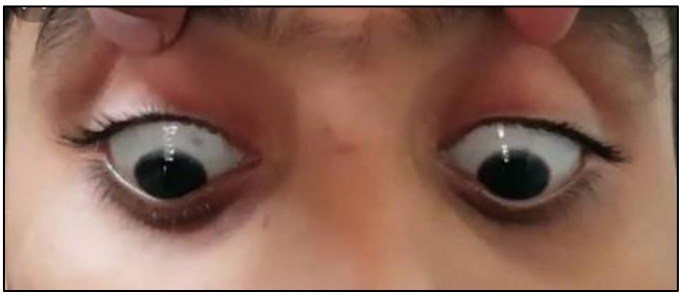

Figure (2): Rizzuto's sign[17]

- A scissoring shadow may be elicited by manual retinoscopy that's because the optical path length through the eye is longer along the direction that light travels through the cone apex compared to the surrounding peripheral region.
- Charleux oil droplet sign[17]: Using the direct ophthalmoscope may reveal this sign **(Figure 3).**

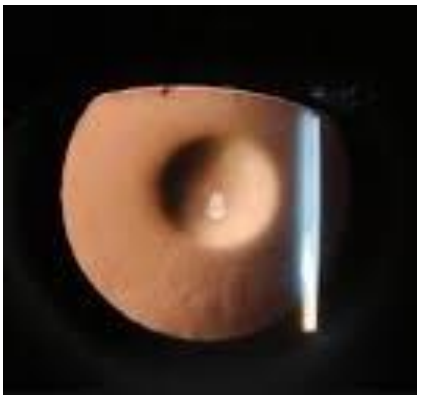

Figure (3): Oil Droplet[17]

*The slit lamp examination reveals some clinical signs such as;

- Focal thinning of the cone apex which is often detected in the lower cornea, using an optical cross-section produced by a thin slit beam under high magnification **(Figure 4).**

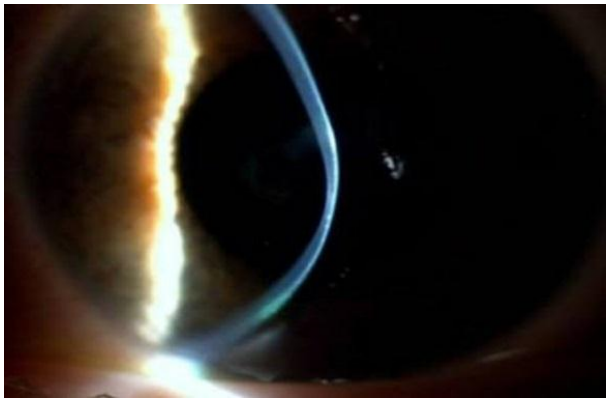

Figure (4): Focal thinning[18]

- Fleischer's ring is due to accumulations of ferritin particles in corneal basal epithelial cells. In normal corneas, ferritin particles are randomly and diffusely scattered throughout the corneal epithelium and basal cells of the conjunctiva, but are not found in corneal stroma or endothelium[19] **(Figure 5)**.

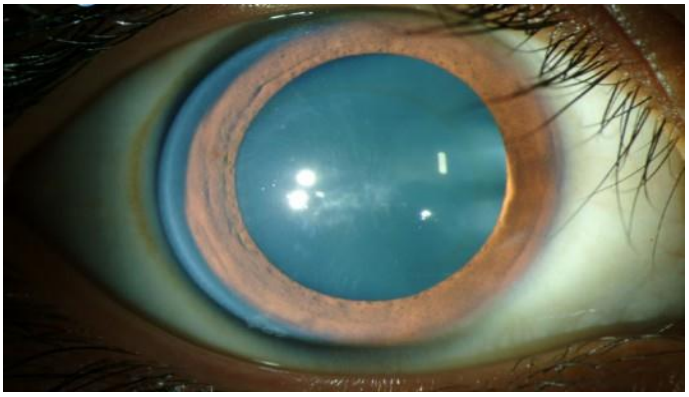

Figure (5): Fleischer's ring[19]

- Vogt's striae[19] as the cornea continues to thin and bulge out stretch marks often develop in the form of anterior stromal scars. Their size or location determines its impact on visual function. They are a sign of corneal stretching and protrusion. They are thin, bright vertical lines located in the deep stroma. They are explained by an increase in the light reflectivity that occurs from changes in relative refractive index in stromal collagen that is under shearing tension from increased strain **(Figure 5)**.

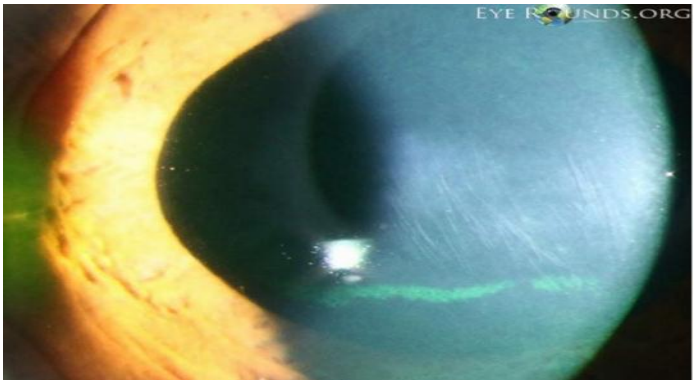

Figure (6): Vogt's striae[19]

- Hydrops if stretching becomes excessive, a tear in Descmets' layer may occur which allow aqueous to access the corneal stroma resulting in corneal edema and acute blurred vision since most of the tears occur centrally. When the endothelium migrates to cover the tear, edema starts to resolve and a posterior scar forms[20] **(Figure 7)**.

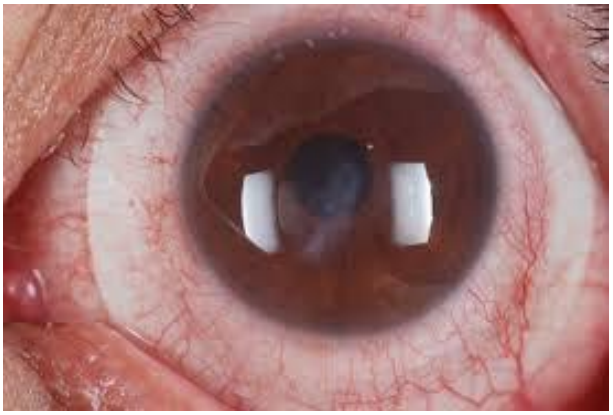

Figure (1): Hydrops[20]

Chapter (2): Role of Pentacam in Diagnosis of KC

Pentacam is a multipurpose, fast and non-contact device used to investigate the anterior segment of the eye. It combines a rotating Scheimpflug camera with a static camera to acquire multiple photographs of the anterior segment to generate the Scheimpflug images in three dimensions[21]. On the Pentacam, the Scheimpflug camera rotates 180 degrees around a single point of fixation as the patient focuses on a central light source. By rotating around the point of fixation, it reduces the artifact created by small movements during image acquisition. In addition, the Pentacam contains a second camera that detects any residual eye movements, which are corrected for by the Pentacam software.

When more than one of the following criteria is found, any of the above mentioned patterns is considered as frank KC, Forme Fruste KC, early stage KC, or at least a case of suspicion according to the severity and amount of signs:

On the sagittal map:

a) K-readings > 48 dpt

b) Skewing of the steepest radial axes (SRAX) > 22º

c) Superior– inferior difference (S-I) on the 5 mm circle > 2.5 dpt

d) Inferior–Superior difference (I-S) > 1.5 dpt

e) Corneal astigmatism on either surface should not be higher than 6D; otherwise, it is a risk factor

f) Against the rule, astigmatism is considered suspicious.

On the thickness map:

a) Cone-like shape

b) Superior–inferior at 5 mm circle > 30 micro

c) Thinnest location < 470 micro

d) Thickness at pachy apex – thickness at thinnest location > 10 micro

e) Y coordinate value of the thinnest location > −500 micro

f) Difference in thickness between both eyes at thinnest locations > 30 micro.

On the elevation maps:

a. Isolated island or tongue-like extension best fit sphere mode (BFS) on either surface.

b. Values > 12 m within the central 5 mm on the anterior elevation map best fit toric ellipsoid (BFTE mode)

c. Values > 15 m within the central 5 mm on the posterior elevation map (BFTE mode)[22]. It is asserted that

posterior surface maps show earlier signs of ectasia that can be seen on the anterior surface via Placido disk topography, but studies have yet to prove this claim due to a wide range of confounding corneal variables[23]. Recent studies show that taking the diagnostic indices of both corneal surfaces into account significantly improves the sensitivity and specificity of keratoconus diagnosis.

Wavefront Analysis:

KC creates significant visual problems derived from the corneal irregular astigmatism. Corneal aberration evaluation helps to describe the optical quality of the cornea and the measurement of the total ocular wavefront aberration provides a reliable tool to detect early KC and to follow its progression [24.25]. Corneal high-order aberrations are significantly increased in KC compared to normal corneas surface illustrates wavefront principle. Zernike analysis describes wavefront analysis of ocular refractive.

The Dutch physician and Nobel Prize winner Fritz Zernike (1888-1966) succeeded in mathematically representing the deviations of a real wavefront from an ideal one expressed as symbols in the radial and angular directions depending on the analysis of the scientist Fourier[26] **(Figure 8)**.

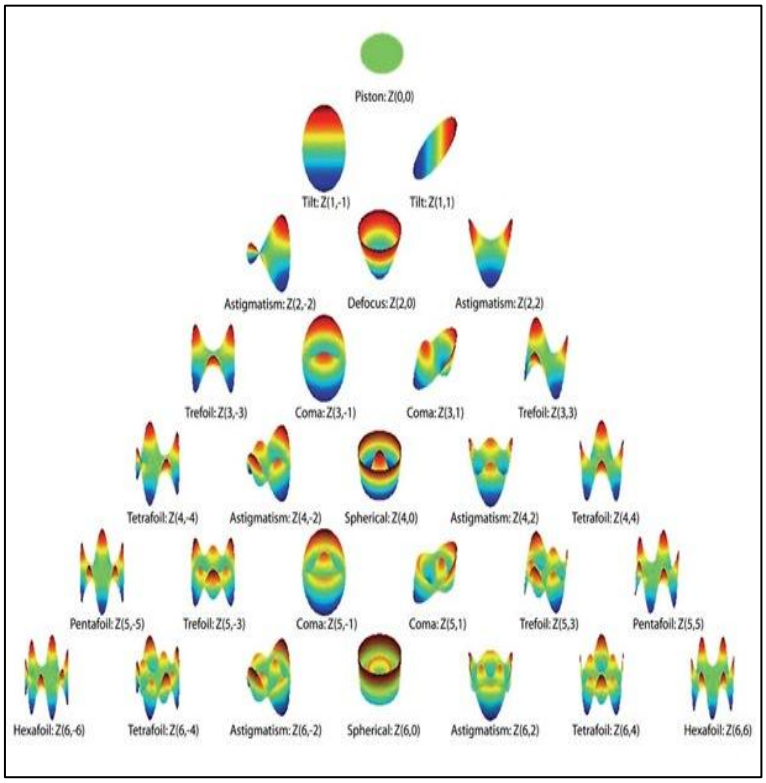

Figure (8): Zernike polynomials ***(Schwiegerling, 2002)***[27]

Following are the most common and important aberrations:

1. Spherical aberrations **(Figure 9)**: They result from abnormal Q-value and affect peripheral vision.

2. Coma **(Figures 10)**: It results from corneal asymmetryin central cornea and affects central vision.

3. Astigmatic high order aberrations (multifoil aberrations) **(Figures 12)**: They result from peripheralasymmetry and affect peripheral vision.

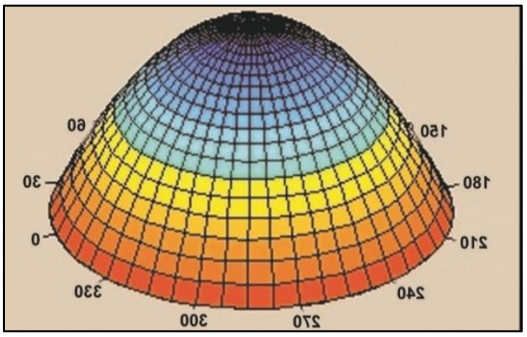

Figure (9): Spherical aberrations. They affect peripheral vision and cause night glare[26]

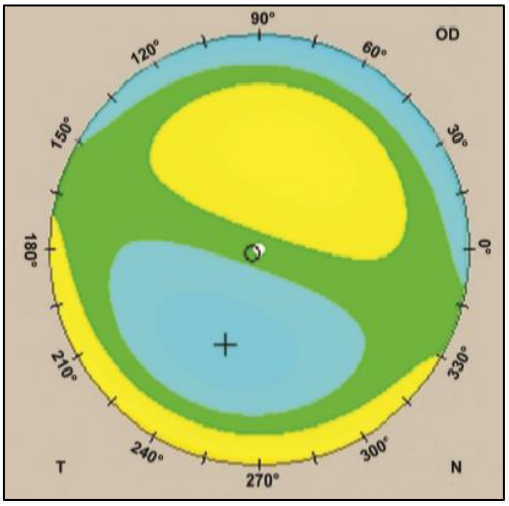

Figure (10): Coma, 2D display. The coma affects central vision[26]

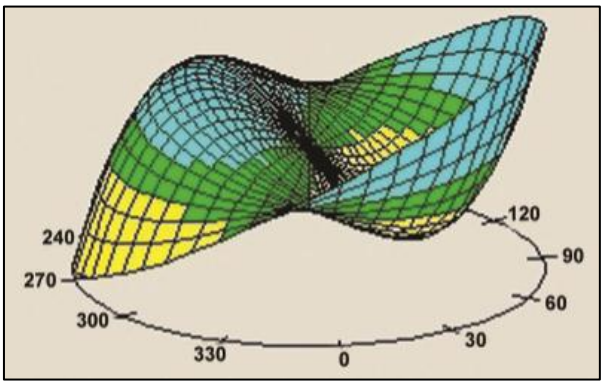

Figure (11): Coma-3D display[26]