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Research Article

Nagy scale vs score for topographic Orbscan diagnosis of Kc

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Abstract

Purpose: Evaluate the sensitivity and specificity of Nagy scale for KC diagnosis by Orbscan11z topography data and compare it with score topographic diagnosis.

Methods: Prospective study of 240 eyes of 145 Patients 95 bilateral and 50 unilateral of KC and Kc suspect were included in this study in the last 2 years. Orbscan 11 Z C. Topography was done to measure the C. thickness, C. power and posterior elevation. I-S value, 3 and 5 mm surface irregularity difference between central thickness and thinnest point and distance of thinnest point from center of the cornea.

Results: Overall sensitivity 78% and specificity were 96% of Nagy scale and it was 67% sensitivity and 90% specificity in score. Nagy scale was more accurate for detection of early and subclinical KC with asymmetrical bow-tie with skewed axis, high astigmatism) [e.g. KC suspect] than score especially in cases of high K reading and abnormal 5 mm surface irregularity that was not detected by score and that was not detected by score and its sensitivity and specificity reach up to 88% and 98 % in early and subclinical KC. There was 15% false negative Kc by score and about 12% false positive Kc and 20% no result by score and detected by Nagy scale.

Conclusion: Nagy scale is more accurate, more sensitive and specific for evaluating subclinical, clinical and advanced Kc than score Orbscan topographic diagnosis and is reliable, very accurate tool especially for evaluating sub clinical and KC suspect cases.

Keywords: *Nagy Scale; Score; Orbscan; C Topography and KC*

Introduction

Keratoconus is a progressive non-inflammatory thinning and ectasia of the cornea of unknown course [1]. It tend to be bilateral but asymmetrical, involving the infero-central portion of the cornea [2]. It affect the central vision relatively early, become manifest in the first three decades and results in progressive visual impairment due to highly irregular myopic astigmatism [3]. In advanced cases, the involved area takes the shape of a truncated cone and can be seen as Munson's sign on down gaze [4,5].

Corneal topography can portray the entire cornea as a surface relief map and producing a color coded picture demonstrating any abnormalities in central, mid peripheral or peripheral curvature [5]. KC is a relatively rare, incidences of KC varies between 50 - 230 per 100,000 of general population about 1 per 2000 [2]. But the incidence increased now [2]. KC may be seen in certain systemic diseases such as Down's syndrome, Marfan's syndrome and Leper's familial amaurosis, Ehlers- Danlos syndrome and mitral valve prolapse [6-8]. It has been noted in people with atopic allergies and those individuals who rub their eyes vigorously [7,9].

A genetic predisposition to Kc has been observed with family history in 6 - 10% [7,8]. Quantitative and qualitative measurements can be detected [5]. There is often photophobia and decreasing corneal sensation, rarely increased visibility of corneal nerves [10]. Occasionally there is a rupture in decrement's membrane giving rise to acute hydrops [11]. The early and rapid diagnosis of Kc minimizes

patient uncertainty and allows for appropriate selection of the option of treatment. Keratectomy becomes highly irregular and of limited information, the placido disk and photokeratoscope gives more information [12].

Corneal topography through computerized photokeratoscope (Orbscan) slit scanning topography and pachymetry system, can detect early cases even subclinical cases (Nagy's line) in asymmetrical bow-tie to differentiate it from clinical Kc [13]. Normal center of the cornea is step and has different patterns (symmetrical bow tie rounded, oval, asymmetrical bow tie (hour glass) or irregular pattern [5,13].

Classification of Keratoconus

Morpology

Classically, keratoconus has been classified into [14,15]:

1. **Nipple:** The cone has a diameter ≤ 5 mm, round morphology and is located in the central or paracentral cornea.
2. **Oval:** The cone has a diameter > 5 mm and a paracentral to peripheral location.
3. **Keratoglobus:** The cone is located throughout 75% of the cornea.

Normal corneas have characteristic patterns of topography. The five original classification categories for normal corneas were described by Bogan., *et al.* [16] and include round, oval, symmetric bow tie, asymmetric bow tie, and irregular. The classification introduced by Rabinowitz., *et al.* [17] added five new categories for normal corneas, with the categories for superior steepening, inferior steepening, and bow tie expanded to include symmetric bow tie with skewed radial axes, asymmetric bow tie with skewed steep radial axes above and below the horizontal meridian (AB/SRAX), asymmetric bow tie with superior steepening, and asymmetric bow tie with inferior steepening (Figure 1). Only 1 in 195 normal patients have mild topographic features similar to, but milder than, those seen in clinically detectable.

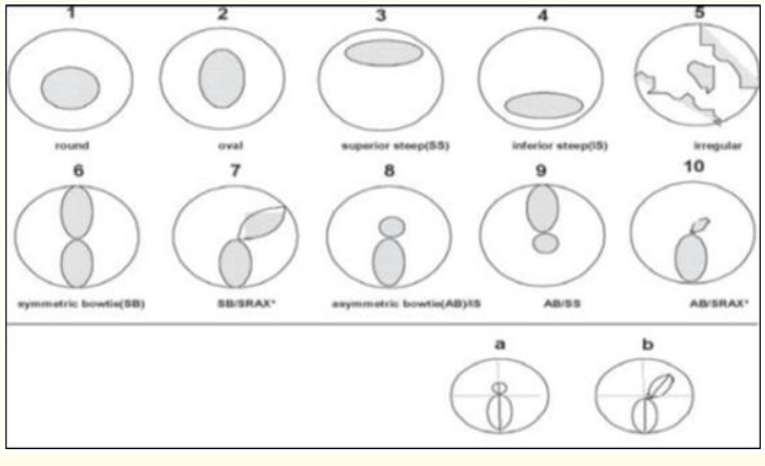

Figure 1: *Classification categories (1-10) for normal corneas. The skewed radial axes (SRAX) pattern suggests there is skewing of the steepest radial axes above and below the horizontal meridian. To interpret this as such, an imaginary line is drawn to bisect the upper and lower lobes of asymmetric bow tie. a) If there is no deviation from the vertical meridian, there is no skewing, and the pattern is labeled AB. b) If the lines bisecting the two lobes appear skewed by more than 30° from the vertical meridian, it is called skewed, and this pattern is labeled AB/SRAX [3].*

Classification based on clinical and topographic indices:

A classification scheme to form a basis for detecting subclinical keratoconus [18]:

1. **Keratoconus:** Stromal corneal thinning by slit-lamp evaluation accompanied by 1 or more of the following clinical signs: Vogt striate, iron ring, Munson sign, scissoring on retinoscopy.
2. **Early keratoconus:** No slit lamp findings of keratoconus; scissoring on retinoscopy only and an asymmetric bowtie (AB) with a skewed radial axes (SRAX) (i.e. AB/SRAX) pattern on corneal topography.
3. **Keratoconus suspect:** No slit lamp findings, no scissoring on retinoscopy, and AB/SRAX pattern corneal topography only.
4. **Normal:** No clinical signs of keratoconus, no scissoring on retinoscopy, and no AB/SRAX pattern on corneal topography.

Topographic classification (Nagy-El Aswad classification)

A new topographic classification of KC (Nagy-El Aswad classification) in to 3 grades of mild, moderate and severe KC has been developed according to these orbscan topographic parameters: Corneal power, Degree of posterior ectasia and corneal thickness [19].

Keratoconus grades according to Nagy-El Aswad classification

1. Grade 1, Mild KC
   a. Corneal power: 44 - 47 diopters (D).
   b. Degree of posterior ectasia: 55 - 75 µm.
   c. Corneal thickness: 450 - 500 µm.
2. Grade 2, Moderate KC:
   a. Corneal power: 47 - 49 D.
   b. Degree of posterior ectasia: 75 - 100 µm.
   c. Corneal thickness: 380 - 450 µm.
3. Grade 3, Severe KC:
   a. Corneal power: > 49 D.
   b. Degree of posterior ectasia: > 100 µm.
   c. Corneal thickness: < 380 µm.
4. Now it is 5 grades
   a. Mild
   b. Mild to Moderate
   c. Moderate
   d. Moderate-to- sever
   e. Sever.

Krumeich keratoconus classification

Keratoconus classification by Krumeich and coauthors [12]. 4 grades of Kc.

Topographic diagnosis of keratoconus

Orbscan IIz in Keratoconus

In clinical keratoconus, Orbscan allows rapid detection and even pattern recognition of typical keratoconus findings.

Stat box assessment

- **Simulated Keratometry (SimK):** The steep SimK and the flat SimK.
- **3 mm and 5 mm zone irregularity data:** The Orbscan usesan algorithm to calculate the corneal irregularity indices in the 3.0 and 5.0 mm zones, which is proportional to the standard deviation of surface curvature. Higher values of the index are indicative of irregular astigmatism and/or higher order aberration, and a threshold of 1.5 D for the 3.0 mm zone and 2.0 - 3.0 D for the 5.0 mm zone can be suggestive of keratoconus [20].

- **Pachymetry of the thinnest point:** And its distance from the visual axis. The location of the thinnest it's located at an average distance of 0.90 mm from visual axis [21,22].
- **Best-fit sphere data:** Corneal surface elevation is measured from a reference, however. This is called best fit sphere (BFS). In corneal ectasia, the earliest signs presumably occur in the posterior cornea.

A posterior BFS value more than 51.0 D has been suggested as an indicator of primary posterior corneal elevation, and a value more than 55.0 D is a criterion for the diagnosis of forme fruste keratoconus (FFKC) [23].

Screening for subclinical keratoconus

Identification of subclinical keratoconus (KC) is a primary concern when screening patients for refractive surgery as performing laser-assisted *in situ* keratomileusis (LASIK) on undiagnosed KC has been identified as the leading cause of ectasia after refractive surgery. However, recognizing subclinical KC is difficult as there is a lack of defined threshold criteria to define this entity [24,25].

In the past, most classification criteria for KC were based on anterior corneal curvature data derived from corneal topography [26,27]. Corneal topography through computerized photokeratoscope can detect early cases even subclinical cases (Nagy's line) in asymmetrical bow-tie to differentiate it from clinical cases (Figure 2). Nagy's line is a horizontal line drawn in the corneal center, any steep area above this line with evidence of asymmetrical bow-tie and high keratoconus prediction index (KPI) indicate subclinical KC [19,28].

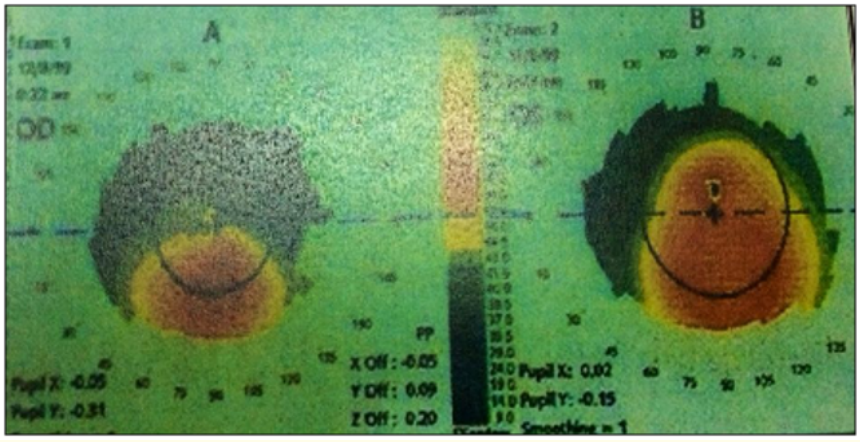

Figure 2: *Nagy's line to differentiate clinical from subclinical KC [28].*

In 2009, Gatinel D and Saad used the data provided by the Orbscan to develop a clinical decision tool to address the specific challenge of early subclinical KC detection, Screening Corneal Objective Risk of Ectasia (SCORE) analyzer. The results of their studies confirmed the combination of placido, elevation and tomography data is a more sensitive and specific detector of early subclinical KC than either placido-disk topography or elevation alone [29,30].

The score analyzer

The score analyzer concept aims to provide the clinician with a unique number to scale the ectasia susceptibility. It is specially designed for myopic eyes. The optimal cut-off value is zero. A positive score (> 0) is predictive of keratoconus-suspect, while a negative score (< 0) is predictive of a normal cornea.

The higher the positive score, the more closely the topographic characteristics of the cornea examined resemble those of keratoconus, and vice versa. The score display (Figure 3), offers a Quad map, a Radar map [29,30].

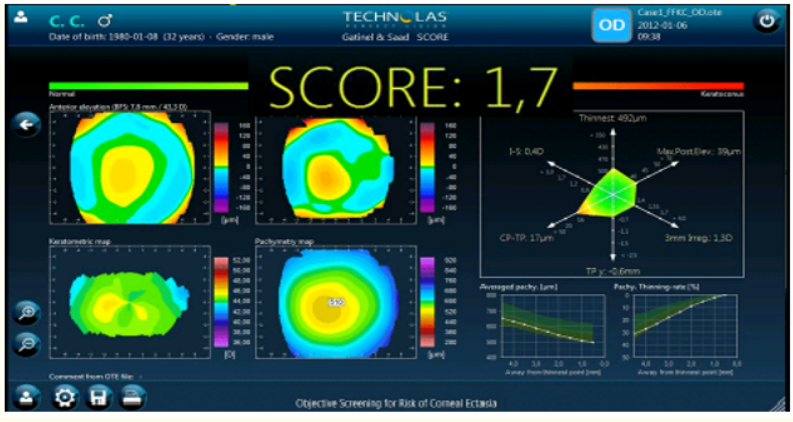

Figure 3: *The SCORE display of the right eye of a patient with left eye advanced keratoconus. Inspection of the maps (Quad Map) reveals the presence of slightly irregular inverse astigmatism and mean central corneal thickness slightly less than the mean (510 microns). The Radar map accentuates the difference between mean central pachymetry and thinnest point. The score is positive [30].*

Radar map

The radar map represents 6 of the most discriminant topographic indices used for calculation of the score (Figure 4). A colour scale ranging from green to red allows rapid visual analysis of the results. Yellow corresponds to the cut-off value.

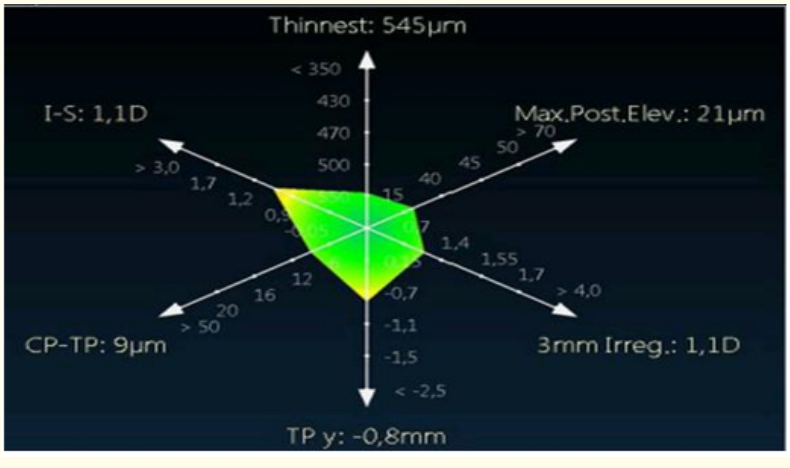

Figure 4: *Radar Map.*

Variables used for construction of the radar map:

1. Pachymetry of the thinnest point (microns): The minimum thickness of the corneal wall.
2. Maximum posterior elevation (microns).
3. Irregularity (diopters) in the central 3 mm.
4. Vertical decantation of the thinnest point (mm): Displacement of the thinnest point in relation to the geometrical center of the cornea.
5. CP-TP: Difference between mean central pachymetry and the pachymetry of the thinnest point.

6. I-S value (diopters): Which corresponds to the difference between mean keratometric values of 5 equidistant points situated 1.5 mm from the vertex on the superior (S) and inferior (I) anterior corneal surface. It reflects the degree of vertical asymmetry of the anterior corneal surface [29,30].

In a study by Chan., *et al.* [30] they have measured the sensitivity and specificity of the score analyzer to detect forme fruste KC in the fellow eyes of patients with frank KC in the other eye. The sensitivity and specificity were 70.8% and 98.1% respectively. Score was negative in 7 eyes (false negative) in the FFKC group (24 eyes) and was positive in 2 eyes (false positive) in the normal control group.

Aim of the Work

The aim of this work was to measure the sensitivity and the specificity of Nagy scale and score measured by the Orbscan11z in diagnosis of clinical and subclinical keratoconus.

Material and Methods

Patients

This study was designed as a prospective comparative clinical study. This study was carried on in Tanta university and Nour-El-Ein private hospital in Tanta for 2 years period from 2016 - 2018. Followed the rules of the Declaration of Helsinki. The nature of the KC disease, were fully explained to all patients. Furthermore, all patients signed written consents approving the procedures and approving the use of their medical data in scientific research work.

This study included 240 eyes of 145 Patients 95 bilateral and 50 unilateral of KC were included in this study. Orbscan 11 Z C. Topography was done to measure the C. thickness, C. power and posterior elevation. I-S value, 3 and 5 mm surface irregularity, difference between central thickness and thinnest point and distance of thinnest point from center of the cornea. The main objectives of this study were to compare between the results of Nagy scale and score topographic analysis of KC and Kc suspect.

Inclusion criteria

1. **Age:** 15 - 35y old.
2. **Sex:** Both sexes were included.
3. **Eyes in the study are classified as follows:**
   a. **Keratoconus:** Stromal corneal thinning by slit-lamp evaluation accompanied by 1 or more of the following clinical signs: Vogt striae, iron ring, Munson sign and scissoring on retinoscopy, as well as abnormal topographic pattern (a localized area of increased surface power, inferior-superior power asymmetry, and skewed steep radial axes above and below the horizontal meridian).
   b. **Keratoconus suspects:** No slit-lamp findings, no scissoring on retinoscopy, but the corneal topography shows: an asymmetric bowtie (AB) with a skewed radial axes (SRAX) (i.e. AB/SRAX) and/or an area of central, inferior or superior steepening combined with oblique cylinder > 1.5 diopters (D) or steep keratometric curvature greater than 47D.
   c. **Normal:** No clinical signs of keratoconus, no scissoring on retinoscopy, and no AB/SRAX pattern on corneal topography. In the normal group the only ocular problem was the refractive error.

Exclusion criteria

- Cases with any ocular pathology such as dry eye, glaucoma, retinal disease, prior ocular surgery, extensive corneal scarring, or systemic diseases such as diabetes and connective tissue disorders.
- Pellucid marginal degeneration.
- For contact lens wearing patients, they were asked to stop wearing contact lenses for minimal period of one month for rigid contact lenses and two weeks for soft contact lenses before assessment. After stopping contact lens use for the recommended period, Patients who still showed apparent corneal warping were also excluded.

Methods

The study was conducted as a prospective case control study. All patients were appropriately informed before their participation in the study, and gave their written informed consent in accordance with institutional guidelines, according to the Declaration of Helsinki.

Every patient included in the study was subjected to:

A detailed ocular and medical history with special attention on:

1. Previous refractive documents and glasses:
   a. History of contact lenses.
   b. Previous ocular surgical interference.
   c. History of relevant systemic disorders.
   d. Family history of keratoconus.
2. Full ophthalmologic examination:
   a. Uncorrected visual acuity (UCVA) using high contrast snellen visual acuity testing and then converted to logMAR scale values.
   b. Subjective refraction (sphere, cylinder, axis, spherical equivalent).
   c. Best corrected visual acuity (BCVA) using high contrast snellen visual acuity testing and then converted to logMAR scale values.
   d. Keratometric readings.
   e. Slit lamp examination of the anterior segment of the eye.
   f. Dilated fundus examination.
   g. Intraocular pressure measurements using applanation tonometry "Goldmann".
3. Corneal Topography: With corneal topographic color-coded maps keratoconus appears topography alone. Therefore, it has been recommended that maps that look suspicious for keratoconus in the presence of a clinically normal eye be labeled "keratoconus suspect" until progression to keratoconus can be documented).
4. Orbscan IIz slit-scanning topography and pachymetry system (Baush and Lomb, Rochestar, NY, USA.

The procedure

The examination process with the Orbscan, similar to other computerized topography systems, the operator visualizes a real-time image of the patient's eye on the computer screen (Figure 5). This is done in a scanning fashion at an angle of 45 degrees, and the backscattered light is captured by a digital video camera. Data from 240 points are extracted from each slit for a total more than 9000 points, then these data are processed by the software to calculate the different variables.

Figure 5: *The Orbscan slit-scanning topography and pachymetry system.*

All participants were examined by the Orbscan IIz slit-scanning topography and pachymetry system by a single trained, experienced examiner. For every eye the refractive map display (Quad map) was chosen and these maps were studied and the following parameters were extracted and statistically analyzed: Anterior best-fit sphere power (D), Anterior best-fit sphere radius (mm), Posterior best-fit sphere power (D), Posterior best-fit sphere radius (mm).

The score analyzer display provides 3 additional graphs to the classic Orbscan quad-map display: the score bar, which visually locates the score value on a linear color scale bar, the radar map display, which is a new visually appealing and efficient map to help the clinician to appreciate the value of 6 pertinent corneal topography derived indices, and the averaged pachymetry and pachymetry thinning curves, which provide meridionally-averaged cross sectional analysis of the corneal thickness profile). The score analyzer display was studied in all eyes and also Nagy scale was studied in all eyes.

New "Nagy Scale" diagnosis of KC Screening of corneal abnormal level of ectasia:

1. C.Power.
2. C.Thickness.
3. Degree of Post. ectasia.
4. mm irregularity.
5. mm irregularity.
6. Distance between thin point and center of the cornea (TP-y).
7. Difference between central thickness and thinnest point (CP-TP).
8. I-S Value.

Statistical methodology

Data were collected and entered to the computer using SPSS (Statistical Package for Social Science) program for statistical analysis (ver 21) [31]. Data were entered as numerical or categorical, as appropriate.

When Kolmogorov-Smirnov test revealed no significance in the distribution of variables, parametric statistics was carried out, while in the not-normally distributed data the non-parametric statistics was carried out [32]:

- Data were described using minimum, maximum, mean, standard deviation and 95% CI of the mean for the normally distributed data.
- Data were described using minimum, maximum, median and inter-quartile range for not-normally distributed data [33].
- Categorical variables were described using frequency and percentage of total.

Sensitivity

Sensitivity = a/a+c

= a (true positive)/a+c (true positive + false negative)

= Probability of being test positive when disease is present.

Specificity

The ability of a test to correctly classify an individual as disease-free.

Specificity = d/b+d

= d (true negative)/b+d (true negative + false positive)

= Probability of being test negative when disease is absent.

Results

Patients demographics

This study included 240 eyes of 145 Patients 95 bilateral and 50 unilateral of KC and KC suspect were included in this study. At the start of the research the KC suspect were 200 eyes and 40 were diagnosed as early KC between the KC suspect (200) 10 diagnosed as normal and 162 were diagnosed as subclinical KC and 28 diagnosed as KC by nagy scale. So after diagnosis, KC suspect become 0 and KC become 40+28 = 68 and subclinical KC become 162 and 10 normal as shown in table 1. So finally after using Nagy scale and score there were figure 6.

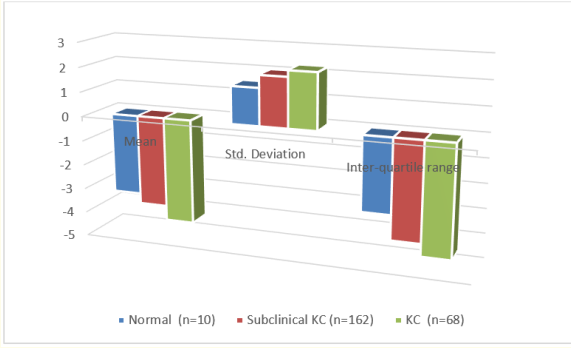

Figure 6: *Mean age of the patients.*

	Pre diagnosis	Post diagnosis
Normal	0	10
KC suspect	200	0
KC	40	68
Subclinical Kc	0	162
Total	240	240

Table 1: *Patients demographic.*

Unilateral or bilateral cases

10 normal 2 bilateral and 6 unilateral, 162 subclinical KC 73 bilateral and 16 unilateral and 68 KC (40 from the start and 28 diagnosed as KC 20 bilateral and 28 unilateral total of 240 eyes 95 bilateral and 50 unilateral. The mean age was in all groups 26.8 ± 8.2 (years). While the range was 18.5 - 35y the mean age of our study participants was 25.1 ± 2.8 (years), 27.20 ± 7.3 (years) and 28.1 ± 5.7 (years) in the normal group, subclinical group and keratoconus group respectively (Table 2 and Figure 6).

	All groups	Normal	Subclinical KC	Kc
Mean age	26.8	25.1	27.2	28.1
SD	8.2	2.8	7.3	5.7

Table 2: *Mean age of the patients.*

Sex

(109) about 75% (75.1%) female and (36) about 25% (42.9%) male of total 145 patients.

Sex	Number	%
Female	109	75%
Male	36	25%
Total	145	100%

Table

Subjective refraction (sphere) (Diopter (D)

The mean of the spherical power of subjective refraction was -3.25 ± 1.5 (D), -3.66 ± 2.0 (D) and -4.25 ± 2.25 (D) in the normal, subclinical and keratoconus group respectively. While the median and IQR were -3.25 (IQR: -4.75 - -1.75D) in the normal group, -3.66 (IQR: -5.66 -1.66 D) in the subclinical group, and - 4.25 (IQR: -6.5 - -2.0 D) in the KC group. There was no statistically significant difference between the three groups (X^2 = 1.95, p = 0.37) (Table 3 and Figure 7).

	Normal (n = 10)	Subclinical KC (n = 162)	KC (n = 68)
Mean	-3.25	-3.66	-4.25
Std. Deviation	1.5	2.0	2.25
Inter-quartile range	-4.75 - -1.75	-5.66 - -1.66	-6.5 - -2.00
Test of Significance (p value)	$X^2_{(KW)(df=2)}$ = 1.95 p = 0.37 NS		

Table 3: *Comparison between normal, subclinical and keratoconic eyes regarding subjective refraction (sphere).*

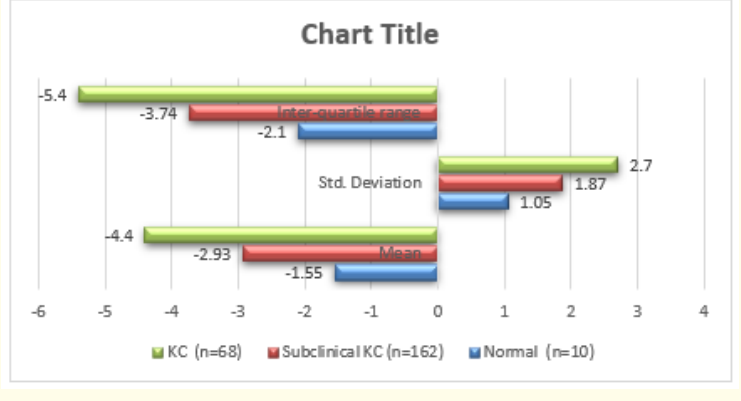

Figure 7

Subjective refraction (cylinder) (diopter)

The mean of the cylinder of subjective refraction was -1.55 ± 1.05 (D), -2.93 ± 1.87 (D) and -4.40 ± 2.70 (D) in the normal, subclinical and keratoconus group respectively. While the median and IQR were -1.55 (IQR: -2.6 - -0.5 D) in the normal group, -2.93 (IQR: -4.8 -1.06 D) in the subclinical group, and - 4.4 (IQR: -7.10 - -1.7 D) in the KC group. There was a statistically significant difference in the cylindrical power of subjective refraction between the three groups (X^2 = 22.548, p = 0.000*) (Table 4 and Figure 8).

	Normal (n = 10)	Subclinical KC (n = 162)	KC (n = 68)
Mean	-1.55	-2.93	-4.40
Std. Deviation	1.05	1.87	2.70
Inter-quartile range	-2.6 - -0.5	-4.8 - -1.06	-7.1 - -1.70
Test of Significance (p value)	$X^2_{(KW)(df=2)} = 22.55$ p = 0.000*		

Table 4: *Comparison between normal, subclinical and keratoconic eyes regarding subjective refraction.*

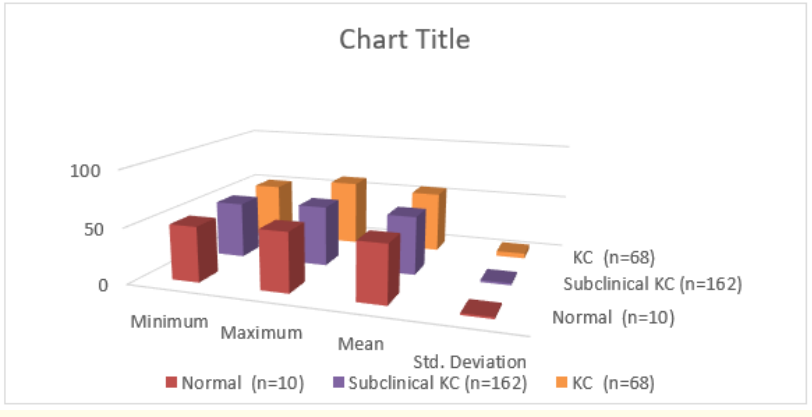

Figure 8

Uncorrected visual acuity (UCVA) (Log MAR)

The UCVA ranged from 0.00 to 1.90 with a mean of 0.95 ± 0.53 in the normal group. in the subclinical group, the UCVA ranged from 0.30 to 1.80 with a mean of 1.05 ± 0.42. In KC group UCVA ranged from 0.20 to 2.00 with a mean of 1.04 ± 0.53. There was no statistically significant difference in the UCVA between all groups (X^2= 2.438, p = 0.296).

Best corrected visual acuity (BCVA) (Log MAR)

The BCVA showed not normal distribution in the three studied groups, so non-parametric statistics were used. In normal eyes, the mean BCVA was 0.10 (IQR: 0.00 - 0.2), in the subclinical keratoconic eyes, the mean BCVA was 0.15 (IQR: 0.05 - 0.25), while in the keratoconic eyes the mean BCVA was 0.63 (IQR: 0.33 - 0.93). There was a statistically significant difference in the BCVA between the three groups.

Topographic pattern

The topographic patterns with the corneal topography were similar to those obtained by the Orbscan. In the normal group, 10 eyes (70.%) 7 eyes showed symmetric bow-tie pattern (SB) on corneal topography, 2 eyes (20%) showed asymmetrical bow-tie with inferior steepening (AB/IS), and 1 eyes (10%) showed asymmetrical bow-tie with superior steepening (AB/SS). they were completely normal with negative score values, so they were included in the normal group.

In the subclinical group, most of eyes showed asymmetric bow-tie pattern (AB): 120 eyes (74.2%) showed AB/IS, 32 eyes (19.7%) showed AB with skewed radial axis (AB/SRAX), and 6 eyes (3.77%) showed AB pattern. In the KC group, 4 eyes (2.46%) showed AB/SRAX pattern,).

ORBSCAN derived parameters

Anterior best-fit sphere power (BFS) (diopters)

The mean of the anterior BFS power was 42.1 ± 1.1 (D), 44.2 ± 0.6 (D) and 45.48 ± 3.20 (D) in the normal, subclinical and keratoconus group respectively, while the mean were 42.1 (41.0 - 43.2) D in the normal group, 44.20 (43.60 - 44.80) D in the subclinical group, and 46.48 (43.28 - 49.68) D in the KC group. There was a statistically significant difference in the anterior BFS power between the three groups

Posterior BFS power (D)

The mean of the posterior BFS power was 51.50 ± 1.70 (D), 52.90 ± 1.8 5 (D) and 55.6 ± 4.6 (D) in the normal, subclinical and keratoconus group respectively, while the mean were 51.5 (49.8 - 53.2) D in the normal group, 52.90 (51.05- 54.75) D in the subclinical group, and 55.60 (60.20 - 51.0) D in the KC group. There was a statistically significant difference in the posterior BFS power between the three groups (p = 0.000) (Table 5 and Figure 9).

	Normal (n = 10)	Subclinical KC (n = 162)	KC (n = 68)
Minimum	49.80	51.05	51.00
Maximum	53.20	54.75	60.20
Mean	51.50	52.90	55.60
Std. Deviation	1.70	1.85	4.60
Test of Significance (p value)	p = 0.000*		

Table 5*: Comparison between normal, subclinical and keratoconic patients regarding posterior BFS power (D).*

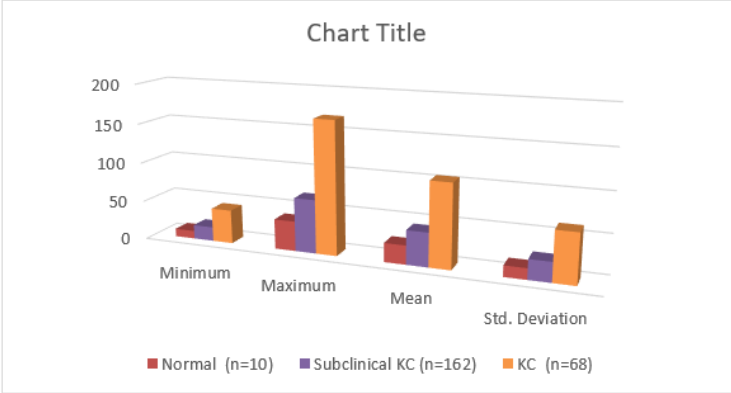

Figure 9

Anterior corneal elevation (anterior difference) (µm)

In normal eyes, the anterior elevation ranged from 4.00 to 20.00 (µm) with a mean of 12.0 ± 8,0 (µm), in the subclinical keratoconic eyes, the anterior elevation ranged from 11.0 to 35.00 (µm) with a mean of 23 ± 12.00 (µm), while in the keratoconic eyes the anterior elevation ranged from 18.00 to 77.00 (µm) with a mean of 47.5 ± 29.5 (µm). There was a statistically significant difference in the anterior corneal elevation between the three groups (p = 0.000).

Posterior corneal elevation (posterior difference) (µm)

In normal eyes, the posterior elevation ranged from 10.00 to 38.00 (µm) with a mean of 24.00 ± 14.0 (µm), in the subclinical keratoconic eyes, the posterior elevation ranged from 18.00 to 68.00 (µm) with a mean of 43.0 ± 25 (µm), while in the keratoconic eyes the anterior elevation ranged from 43.00 to 168.00 (µm) with a mean of 105.5 ± 62.5 (µm) (Table 6 and Figure 10).

	Normal (n = 10)	Subclinical KC (n = 162)	KC (n = 68)
Minimum	10.00	18.00	43.00
Maximum	38.00	68.00	168.00
Mean	24.00	43.00	105.5
Std. Deviation	14.00	25.00	62.5
Test of Significance (p value)	p = 0.000*		

Table 6: *Comparison between normal, subclinical and keratoconic eyes regarding posterior corneal elevation (µm) off the BFS.*

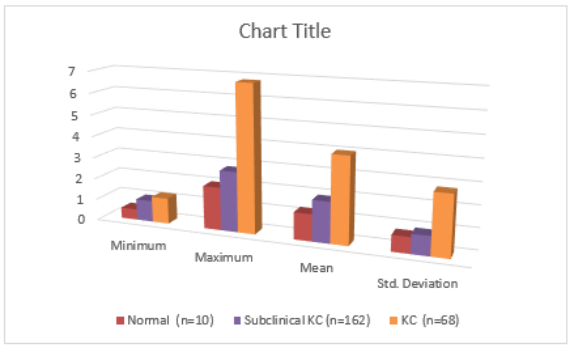

Figure 10

Three mm zone irregularity

Three mm zone irregularity ranged from 0.50 to 2.00 (mm) with a mean of 1.25 ± 0.75 (mm) in normal eyes, while in the subclinical keratoconic eyes, 3 mm zone irregularity ranged from 1.00 to 2.80 (mm) with a mean of 1.9 ± 0.9 (mm). In keratoconic eyes, 3 mm zone irregularity ranged from 1.20 to 6.80 (mm) with a mean of 4.0 ± 1.82 (mm). There was a statistically significant difference between the three groups (p = 0.000) (Table 7 and Figure 11).

	Normal (n = 10)	Subclinical KC (n = 162)	KC (n = 68)
Minimum	0.50	1.00	1.20
Maximum	2.00	2.80	6.8
Mean	1.25	1.9	4.0
Std. Deviation	0.75	0.9	2.8
Test of Significance (p value)	p = 0.000*		

Table 7: *Comparison between normal, subclinical and keratoconic eyes regarding 3 mm zone irregularity.*

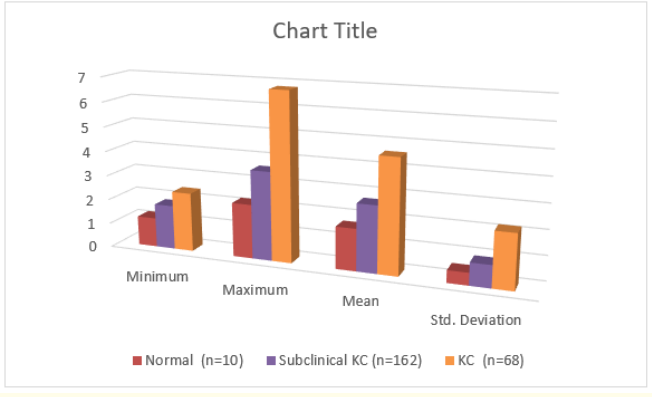

Figure 11

Five mm zone irregularity

5 mm zone irregularity ranged from 1.2 to 2.2 (mm) with a mean of 1.7 ± 0.5 (mm) in normal eyes, while in the subclinical keratoconic eyes, 5 mm zone irregularity ranged from 1.80 to 3.60 (mm) with a mean of 2.7 ± 0.9 (mm). In keratoconic eyes, 5 mm zone irregularity ranged from 2.40 to 6.80 (mm) with a mean of 4.6 ± 2.2 (mm). There was a statistically significant difference between the three groups (p = 0.000) (Table 8 and Figure 12).

	Normal (n = 10)	Subclinical KC (n = 162)	KC (n = 68)
Minimum	1.2	1.80	2.40
Maximum	2.2	3.60	6.80
Mean	1.7	2.7	4.6
Std. Deviation	0.5	0.9	2.2
Test of Significance (p value)	p = 0.000*		

Table 8: *Comparison between normal, subclinical and keratoconic eyes regarding 5 mm zone irregularity.*

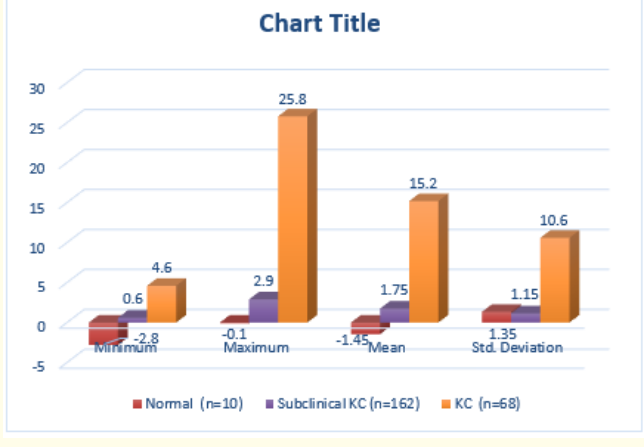

Figure 12

Steep K (D)

The mean steep K ranged from 41.5 to 46.2 (D) with a mean of 43.85 ± 2.35 (D) in normal eyes, while in the subclinical keratoconic eyes, it is ranged from 42.9 to 48.2 (D) with a mean of 45.55 ± 2.65 (D). In keratoconic eyes, it is ranged from 45.9 to 58.2 (D) with a mean of 52.05 ± 6.15 (D). There was a statistically significant difference between the three groups (p = 0.000).

Score value

The score value ranged from -2.80 to -0.10 with a mean of -1.45 ± 1.35 in the normal group. In the subclinical group, the score value ranged from 0.60 to 2.90 with a mean of 1.75 ± 1.15, while in the KC group, it ranged from 4.60 to 25.80 with a mean of 15.20 ± 10.6 there was a statistically significant difference between the three groups (p = 0.000) (Table 9 and Figure 13).

	Normal (n = 10)	Subclinical KC (n = 162)	KC (n = 68)
Minimum	-2.80	0.60	4.60
Maximum	-0.10	2.90	25.80
Mean	-1.45	1.75	15.20
Std. Deviation	1.35	1.15	10.60
Test of Significance (p value)	p = 0.000*		

Table 9: *Comparison between normal, subclinical and keratoconic eyes regarding score value.*

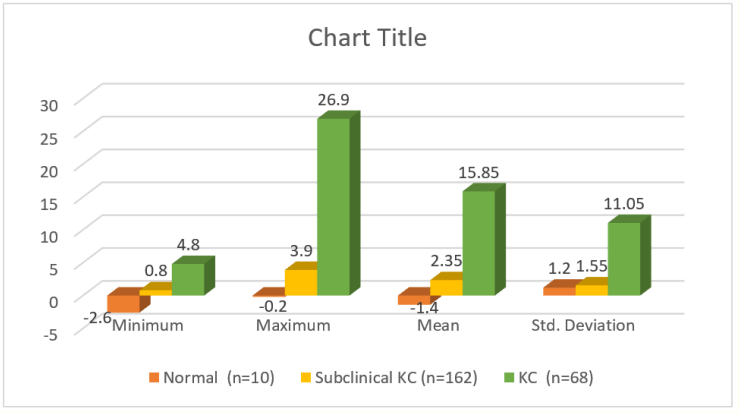

Figure 13

Nagy scale value

The Nagy scale value ranged from -2.60 to -0.20 with a mean of -1.4 ± 1.2 in the normal group. In the subclinical group, the Nagy scale value ranged from 0.80 to 3.90 with a mean of 2.35 ± 1.55, while in the KC group, it ranged from 4.80 to 26.90 with a mean of 15.85 ± 11.05 there was a statistically significant difference between the three groups (p = 0.000) (Table 10 and Figure 14).

	Normal (n = 10)	Subclinical KC (n = 162)	KC (n = 68)
Minimum	-2.60	0.80	4.80
Maximum	-0.20	3.90	26.90
Mean	-1.4	2.35	15.85
Std. Deviation	1.2	1.55	11.05
Test of Significance (p value)	p = 0.000*		

Table 10: *Comparison between normal, subclinical and keratoconic eyes regarding score value.*

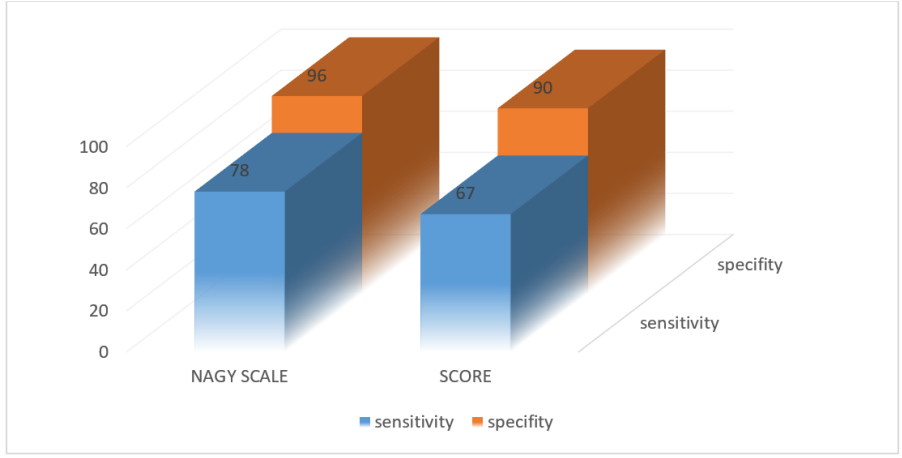

Figure 14

Sensitivity and specificity

Overall sensitivity 78% and specificity were 96% of Nagy scale and it was 67% sensitivity and 90% specificity in score (Table 11 and Figure 15).

	Nagy scale	Score
Sensitivity %	78%	67%
Specificity %	96%	90%

Table 11

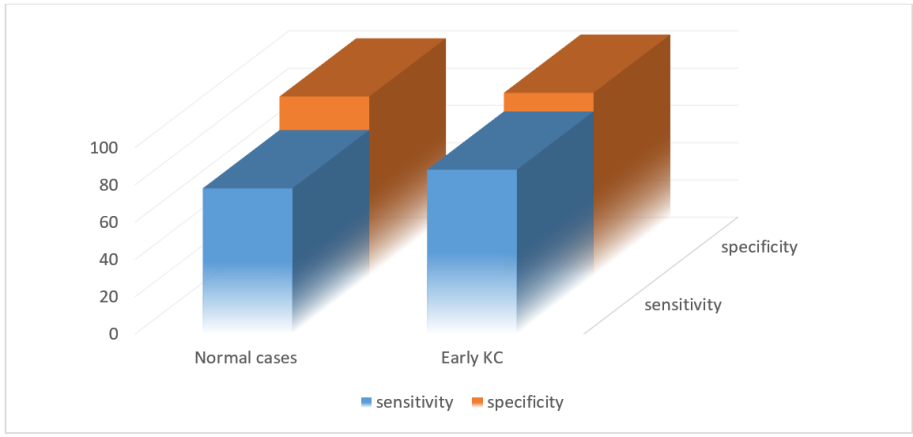

Figure 15

Accuracy

Nagy scale was more accurate for detection of early and subclinical KC with asymmetrical bow-tie with skewed axis, high astigmatism) [e.g. KC suspect] than score especially in cases of high K reading and abnormal 5 mm surface irregularity that was not detected by score and its sensitivity and specificity reach up to 88% and 98 % in early and subclinical KC (Table 12 and Figure 16).

Nagy Scale	Normal cases	Early (subclinical KC)
Sensitivity %	78%	88%
Specificity %	96%	98%

Table 12

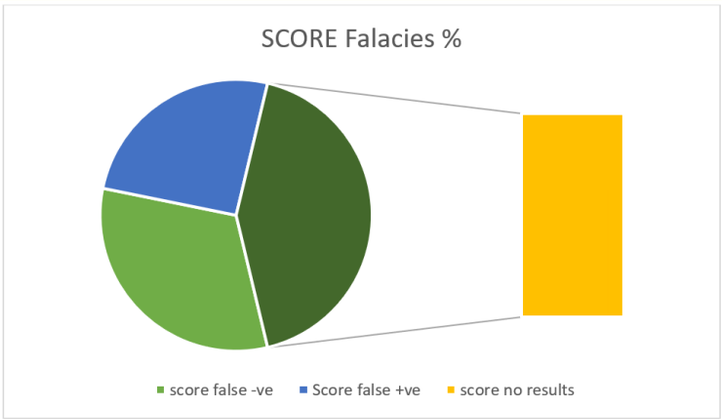

Figure 16

Fallacies of Score

There was 15% false negative KC by score and about 12% false positive KC and 20% no result by score and detected by Nagy scale.

Score False negative	15%
Score False positive	12%
Score No results	20%

Table 13

False positive score

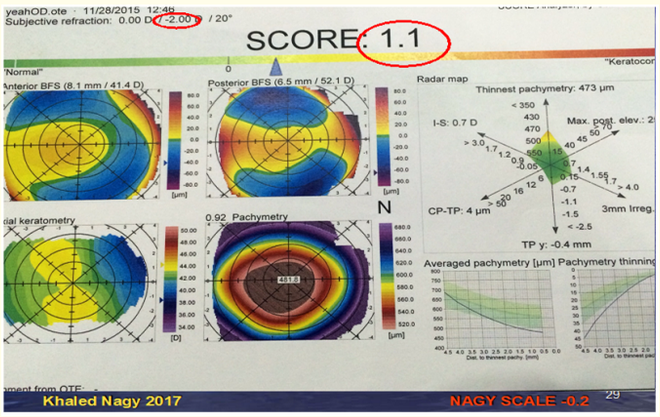

Figure 17: *Score +1.1, Nagy Scale -0.2.*

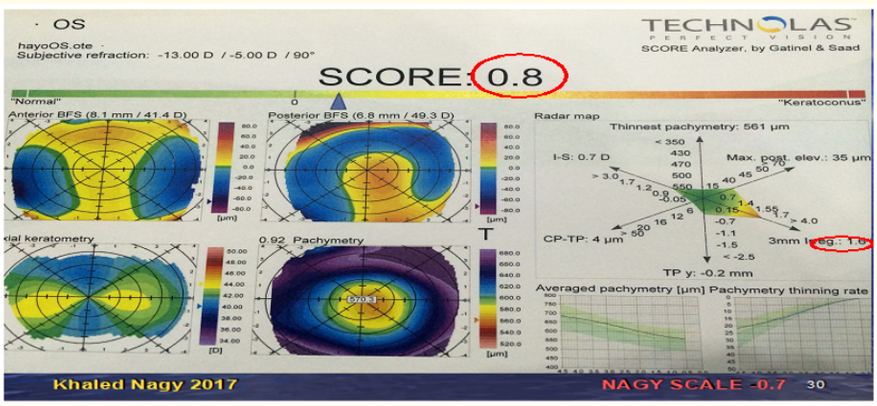

Figure 18: *Score +0.8, Nagy Scale -0.7.*

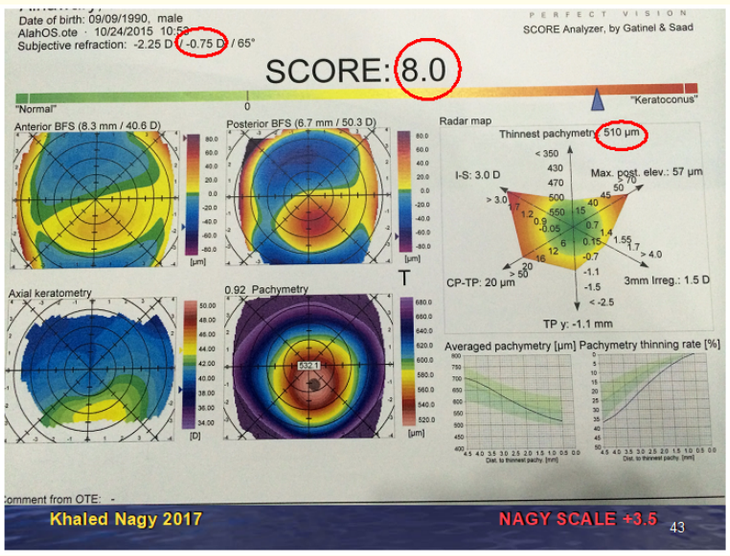

Figure 19: *Score +8.0, Nagy Scale +3.5.*

False negative score

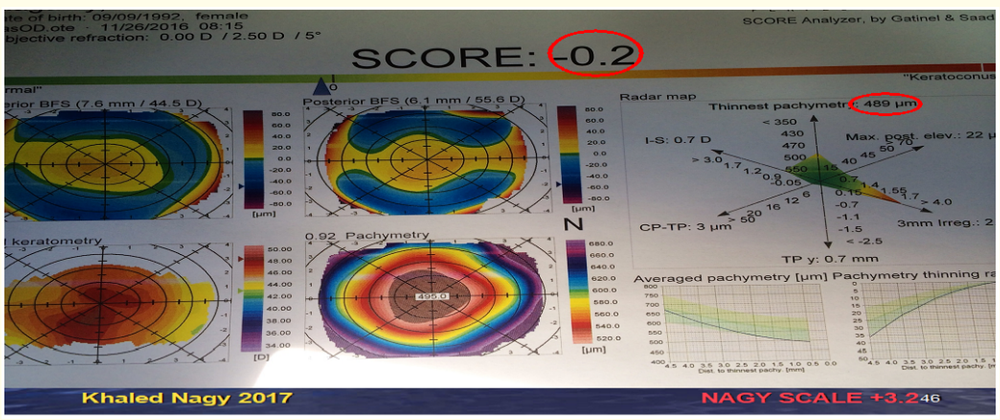

Figure 20: *Orbscan and Score of KC score -0.2, Nagy Scale +3.2.*

undetected score

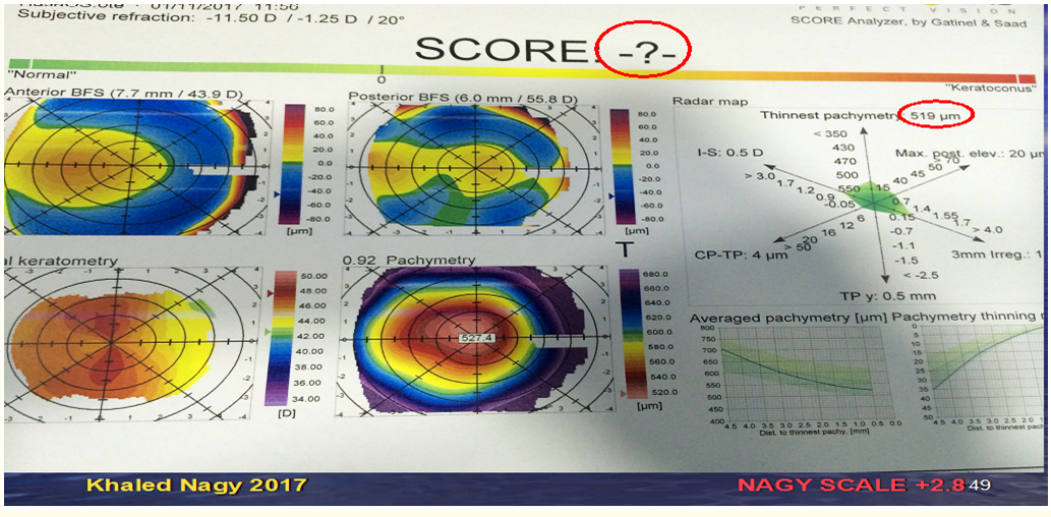

Figure 21: *Orbscan and Score of KC score ?, Nagy Scale*

Discussion

Invention of tomographic imaging as Orbascan has demonstrated that the keratoconus is a posterior corneal disease that starts in the back surface of the cornea. So, posterior corneal imagining is needed for diagnosis of keratoconus and its monitoring [27,34,35].

Identification of subclinical KC is a primary concern when screening patients for refractive surgery as performing LASIK on undiagnosed subclinical KC has been identified as the leading cause of ectasia after refractive surgery [22,35].

We are in need of tomographic finding to classify and stage the disease and to follow up its progression or regression. Also, we should define the most sensitive parameters and their correlation to the disease to both diagnose and detect either its progression with time or regression with treatment.

In a study by Mihaltz., *et al.* indicated that posterior elevation was the most important criterion in the diagnosis of keratoconus [36,37]. The purpose of our study was to determine the sensitivity and specificity of nagy scale and score in discriminating subclinical or clinical KC from normal corneas employing the Orbscan IIz scanning slit topographer. This study included 68 eyes of clinical KC, 162 eyes of subclinical KC and 10 of normal eyes as control.

We studied different parameters of the Orbscan 11z (anterior BFS radius and power, posterior BFS radius and power, anterior corneal elevation, posterior corneal elevation, 3 mm, thinnest point pachymetry, central pachymetry, as score value and steep K and 5 mm irregularity as well as the NAGY scale value) aiming to detect any statistically significant difference in these parameters between our three groups. We used the most modern statistical analysis and the diagnostic test accuracy to detect the sensitivity and specificity of anterior and posterior corneal elevation data measured by the Orbscan 11Z in discriminating subclinical and clinical KC from normal corneas.

The mean age was in all groups 26.8 ± 8.2 (years). While the range was 18.5 - 35y the mean age of our study participants was 25.1 ± 2.8 (years), 27.20 ± 7.3 (years) and 28.1 ± 5.7 (years) in the normal group, subclinical group and keratoconus group respectively, younger than those enrolled in the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study 2007, which was 39.3 ± 10.9 (years) for KC [38]. On the other hand the mean age was similar to those enrolled in a study by Jafarinasab., *et al* [39].

Sex (109) about 75% (75.1%) female and (36) about 25% (42.9%) male of total 145 patients. There was no statistically significant difference between our three study groups in terms of gender. There was no statistically significant difference between our three study groups in terms of the UCVA and the sphere part of subjective refraction. On the other hand, there was a statistically significant difference between them in the BSCVA. In the normal group, BSCVA ranged from 0.18 to 0.00. In subclinical group it ranged from 0.18 to 0.18, and from 0.6 to 0.3 in KC group. In the CLEK study, BCVA was 0.3 or more in 58% of KC patients. In an Indian study, BCVA was 0.3 or more in 30% of KC patients [40].

There was a statistically significant difference between our groups in the cylindrical refractive error. The mean of the cylinder of subjective refraction was -1.55 ±1.05 (D), -2.93 ± 1.87 (D) and -4.40 ± 2.70 (D) in the normal, subclinical and keratoconus group respectively. While the median and IQR were -1.55 (IQR: -2.6 - -0.5 D) in the normal group, -2.93 (IQR: -4.8 -1.06 D) in the subclinical group, and - 4.4 (IQR: -7.10 - -1.7 D) in the KC group. There was a statistically significant difference in the cylindrical power of subjective refraction between the three groups (X^2=22.548).

This correlates with a recent study of Serdarogullari H., *et al.* this study concluded that subjects with astigmatism of 2 D or more attending to outpatient clinics should be screened with corneal topography for early diagnosis even if their visual acuity is not affected [41].

Orbscan derived parameters

There were statistically significant differences between normal, subclinical and KC eyes in all Orbscan parameters.

Keratometric readings

Our findings showed that the mean steep K is significantly higher in KC. The mean steep K ranged from 41.5 to 46.2 (D) with a mean of 43.85 ± 2.35 (D) in normal eyes, while in the subclinical keratoconic eyes, it is ranged from 42.9 to 48.2 (D) with a mean of 45.55 ± 2.65 (D). In keratoconic eyes, it is ranged from 45.9 to 58.2 (D) with a mean of 52.05 ± 6.15 (D). There was a statistically significant difference between the three groups (p = 0.000) Prakash G., *et al.* reported major variables for grading keratoconus (K_{max}, central and minimum corneal thickness (MCT), RMS of HOA) can be linked by linear regression equations to predict the pathologic behavior of keratoconus [42].

Irregularity indices at 3 mm and 5 mm zones

We found a statistically significant difference in irregularity at 3 mm. Three mm zone irregularity ranged from 0.50 to 2.00 (mm) with a mean of 1.25 ± 0.75 (mm) in normal eyes, while in the subclinical keratoconic eyes, 3 mm zone irregularity ranged from 1.00 to 2.80 (mm) with a mean of 1.9 ± 0.9 (mm). In keratoconic eyes, 3 mm zone irregularity ranged from 1.20 to 6.80 (mm) with a mean of 4.0 ± 1.82 (mm).

There was a statistically significant difference between the three groups (p = 0.000) 5 mm zone irregularity ranged from 1.2 to 2.2 (mm) with a mean of 1.7 ± 0.5 (mm) in normal eyes, while in the subclinical keratoconic eyes, 5 mm zone irregularity ranged from 1.80 to 3.60 (mm) with a mean of 2.7 ± 0.9 (mm). In keratoconic eyes, 5 mm zone irregularity ranged from 2.40 to 6.80 (mm) with a mean of 4.6 ± 2.2 (mm). There was a statistically significant difference between the three groups (p = 0.000).

Sonmez., *et al.* [43] reported that the mean of irregularity at 3 mm and 5 mm was (1.04 ± 0.33D, 1.33 ± 0.36 D) in normal and (4.20 ± 2.15 D, 4.50 ± 2.44 D) in KC group. Lim., *et al.* [44] found 3 mm and 5 mm irregularity were higher in KC suspects (2.44 ± 1.36 D, 2.61 ± 1.19 D) than normal eyes (1.05 ± 0.37 D, 1.38 ± 0.39 D).

Pachymetry

Corneal thinning is a key pathological feature of keratoconus. The mean thinnest point pachymetry showed a statistically significant difference between normal (549.92 ± 31.16 μm), subclinical (495.67 ± 25.91 μm) and KC eyes (436.09 ± 50.41 μm). The mean central

pachymetry also showed a statistically significant difference between normal (560.69 ± 35.64 µm), subclinical (508.87 ± 25.35 µm) and KC eyes (462.76 ± 49.64 µm).

Schlegel., *et al.* [25] studied the central and thinnest corneal pachymetries were analyzed and compared using the Orbscan IIz slit-scanning topography. They found that the differences between the keratoconus suspect group and normal group were statistically significant for mean central and thinnest pachymetries. Lim., *et al.* [44] found thinner corneas (mean 504.4 ± 40.4 µm) in keratoconus suspects than normal eyes (mean 554.0 ± 25.0 µm).

Sonmez., *et al.* [43] reported the mean thinnest optical pachymetry values of the Orbsan were (548 µm) in the normal group and (472 µm) in the KC).

Elevation parameters

Previous studies reported that anterior and posterior corneal elevation were the most effective parameters for the diagnosis of keratoconus [45]. In 2012, Ishii and his coworkers investigated the severity of KC in terms of corneal elevation differences, improving keratoconus diagnostic accuracy and in grading the severity of keratoconus [45].

Posterior corneal elevation (posterior difference) (µm)

In normal eyes, the posterior elevation ranged from 10.00 to 38.00 (µm) with a mean of 24.00 ± 14.0 (µm), in the subclinical keratoconic eyes, the posterior elevation ranged from 18.00 to 68.00 (µm) with a mean of 43.0 ± 25 (µm), while in the keratoconic eyes the post elevation ranged from 43.00 to 168.00 (µm) with a mean of 105.5 ± 62.5 (µm) therefore posterior corneal elevation is a useful index for discriminating between these conditions.

Jafarinasab., *et al.* [39] found mean posterior corneal elevation measured by Orbscan IIz to be 106.80 ± 43.98 µm in KC, 36.60 ± 22.80 µm in subclinical KC, and 25.00 ± 9.15 µm in normal eyes. Lim., *et al.* [44] found that the mean values of maximum posterior elevation and were significantly higher in KC and KC-suspect eyes than in control eyes.

Anterior corneal elevation (anterior difference) (µm)

In normal eyes, the anterior elevation ranged from 4.00 to 20.00 (µm) with a mean of 12.0 ± 8,0 (µm), in the subclinical keratoconic eyes, the anterior elevation ranged from 11.0 to 35.00 (µm) with a mean of 23 ± 12.00 (µm), while in the keratoconic eyes the anterior elevation ranged from 18.00 to 77.00 (µm) with a mean of 47.5 ± 29.5 (µm). There was a statistically significant difference in the anterior corneal elevation between the three groups ($p = 0.000$).

Sensitivity is defined as the ability of a test to correctly identify those with the disease (true positive), whereas specificity is defined as the ability of the test to correctly identify those without the disease (true negative rate).

We found that Posterior and anterior corneal elevation in clinical KC are statistically significant discriminators of occurrence with Area under the ROC curve. We found that Posterior and anterior elevation data can discriminate subclinical KC from normal eyes but with less reliability than in clinical KC with Area under the ROC.

In our study, a cutoff point of ≥ 35 µm for posterior elevation to discriminate subclinical KC from normal eyes yielded sensitivity of 86.67% and specificity of 69.23%. Also we revealed that the best anterior elevation cutoff point for discriminating subclinical KC from normal eyes was ≥ 22 microns (µm) with sensitivity of 53.33% and specificity of 88.46%. These figures are relatively less powerful for distinguishing normal from subclinical KC subjects.

Although it has been suggested that an increase in posterior elevation may be the earliest sign of subclinical KC [27], it should not be used alone for differentiating subclinical KC from normal corneas. Nevertheless, in eyes with subclinical KC, the scanning slit topography (Orbscan II) may add further information to placido disk-based videokeratography data.

Lim., *et al.* [44] found that the mean values of maximum posterior elevation and irregularity were significantly higher in keratoconus and keratoconus-suspect eyes than in control eyes. They reported cutoff points of 26 μm and 46 μm for the maximum posterior elevation values in normal eyes and keratoconus-suspect eyes, respectively.

Rao., *et al.* [46] examined 60 eyes of KC suspects with Orbscan II and posterior elevation values. They recommended considering a maximum central posterior elevation of 40 mm or more as a risk factor for forme fruste keratoconus.

De Sanctis., *et al.* [47] evaluated the sensitivity and specificity of PE in discriminating normal corneas from KC. Mean posterior corneal elevation was statistically higher in keratoconus (100.7 ± 49.2 (μm); P < 0.001), and subclinical keratoconus (39.9 ± 15.0 (μm); P = 0.01) versus normal corneas (19.8 ± 6.37 (μm)). The AUROC analyses showed high overall predictive accuracy of PE for KC (AUROC 0.99). Optimal cutoff points were 35 (μm) for keratoconus and 29 (μm) for subclinical keratoconus. These values were associated with sensitivity and specificity of 97.3% and 96.9%, respectively, for keratoconus, and 68% and 90.8% for subclinical keratoconus.

In a study by Jafarinasab., *et al.* [48], mean anterior and posterior corneal elevations were statistically higher in keratoconus and subclinical keratoconus versus normal corneas. The posterior elevation measurement in the 3-mm zone had the strongest power to distinguish keratoconus from normal. The corresponding figure for the 7-mm zone, however, had the strongest power to distinguish eyes with subclinical keratoconus (area under the curve, 0.98 and 0.92, respectively). Optimal cutoff point for posterior elevation in the 3-mm zone was 18.5 μm for keratoconus (sensitivity, 92%; specificity, 95%). The corresponding figure in the 7-mm zone was 50.5 μm for subclinical keratoconus (sensitivity, 79.9%; specificity, 94.0%).

Anterior and posterior corneal elevation data measured by Orbscan II are very effective for discriminating clinical KC from normal corneas, these indices can also differentiate subclinical KC from normal cases but with less reliability than clinical KC. Thus, anterior and posterior elevation results should be combined with other data for evaluation of patients suspected of KC. Thus, the score analyzer was developed. The score is the result of the linear combination of 12 topographic variables that can provide the clinician with a unique number to scale the ectasia susceptibility [29].

In a study by Chac C., *et al.* [30] the SCORE analyzer was found to be valid and consistent in FFKC detection showing good sensitivity and specificity, and to be useful in objectively identifying cases at risk of post-LASIK keratectasia.

The cutoff points provided in our study can be used in clinical settings, particularly among refractive surgery candidates for keratoconus screening with the Orbscan in Egypt. The difference between our best cutoff point for PE to differentiate KC from normal corneas (≥ 46 μm) and the cutoff point reported by Rao., *et al.* and Fam and Lim (≥ 40 μm) could be due to racial differences as well as differences in patient characteristics. Furthermore, the development of relatively new therapeutic modalities that effectively decrease the progression of keratoconus, may be beyond the presentation of the disease in less severe forms. Meta-analysis of multiple studies from multiple centers all over the world is recommended to detect a universal cutoff point for PE to differentiate KC from normal corneas using the Orbscan slit-scanning tomography.

Score value

The score value ranged from -2.80 to -0.10 with a mean of -1.45 ± 1.35 in the normal group. In the subclinical group, the score value ranged from 0.60 to 2.90 with a mean of 1.75 ± 1.15, while in the KC group, it ranged from 4.60 to 25.80 with a mean of 15.20 ± 10.6 there was a statistically significant difference between the three groups (p = 0.000) [30,31].

Nagy scale value

The Nagy scale value ranged from -2.60 to -0.20 with a mean of -1.4 ± 1.2 in the normal group in the subclinical group, the Nagy scale value ranged from 0.80 to 3.90 with a mean of 2.35 ± 1.55, while in the KC group, it ranged from. 4.80 to 26.90 with a mean of 15.85 ± 11.05 there was a statistically significant difference between the three groups.

Sensitivity and specificity

Overall sensitivity 78% and specificity were 96% of Nagy scale and it was 67% sensitivity and 90% specificity in score. De Sanctis., *et al.* [47] evaluated the sensitivity and specificity these values were associated with sensitivity and specificity of 97.3% and 96.9%, respectively, for keratoconus, and 68% and 90.8% for subclinical keratoconus.

Accuracy

Nagy scale was more accurate for detection of early and subclinical KC with asymmetrical bow-tie with skewed axis, high astigmatism) [e.g. KC suspect] than score especially in cases of high K reading and abnormal 5 mm surface irregularity that was not detected by score and its sensitivity and specificity reach up to 88% and 98% in early and subclinical KC.

Summary and Conclusion

1. There was 15% false negative KC by score and about 12% false positive KC and 20% no result by score and detected by Nagy scale overall sensitivity 78% and specificity were 96% of Nagy scale and it was 67% sensitivity and 90% specificity in score.
2. Nagy scale was more accurate for detection of early and subclinical KC with asymmetrical bow-tie and its sensitivity and specificity reach up to 88% and 98 % in early and subclinical KC.
3. Nagy scale is more accurate, more sensitive and specific for evaluating subclinical, clinical and advanced Kc than score Orbscan topographic diagnosis and is reliable, very accurate tool especially for evaluating sub clinical and KC suspect cases.

Bibliography

1. Espandar L and Meyer J. "Keratoconus overview and update on treatment". *Middle East African Journal of Ophthalmology* 17.1 (2010): 15-20.
2. Alió JL., *et al*. "Analysis of results related to good and bad outcomes of Intacs implantation for keratoconus correction". *Journal of Cataract and Refractive Surgery* 32.5 (2006): 756-761.
3. Kennedy R., *et al*. "A 48-year clinical and epidemiologic study of keratoconus". *American Journal of Ophthalmology* 101.3 (1986): 267-273.
4. Macsai M., *et al*. "Keratoconus and Turner syndrome". *Cornea* 16.5 (1997): 534-536.
5. Nagy Kh and Able R. "Keratoconus". In: Roy F, Fraunfelder F (eds). Current ocular therapy, 4th edition. Pheladelphia, WB: Saunders Company (1995-2000): 501-503.
6. McMonnies C. "Abnormal rubbing and keratectasia". *Eye and Contact Lens* 33 (2007): 265-271.
7. Rados A. "Conical cornea and mongolism". *Archives of Ophthalmology* 40.4 (1984): 454-478.
8. Haugen O. "Keratoconus in the mentally retarded". *Acta Ophthalmologica* 70.1 (1992): 111-114.
9. Robertson I. "Keratoconus and the Ehler-Danlos syndrome: A new aspect of keratoconus". *Medical Journal of Australia* 1.18 (1975): 571-573.
10. Nordan LT. "Keratoconus: diagnosis and treatment". *International Ophthalmology Clinics* 37.1 (1997): 51-63.
11. Campbell R and Caroline P. "Identifying characteristics of Keratoconus". *CL Spectrum* 10.4 (1995): 56.
12. Krumeich J., *et al*. "Live-epikeratophakia for keratoconus". *Journal of Cataract and Refractive Surgery* 24.4 (1998): 456-463.
13. Nagy Kh. "Corneal Topography book". 1st edition. Tanta, Egypt: El-qwmia El-Haditha Library (1997).

14. Kinoshita S., *et al*. "Incidence of prominent corneal nerves in multiple endocrine neoplasia type 2A". *American Journal of Ophthalmology* 111.3 (1991): 307-311.

15. Tuft S., *et al*. "Acute corneal hydrops in keratoconus". *Ophthalmology* 101.10 (1994): 1738-1744.

16. Bogan SJ., *et al*. "Classification of normal corneal topography based on computer-assisted videokeratography". *Archives of Ophthalmology* 108.7 (1990): 945-949.

17. Rabinowitz YS., *et al*. "Videokeratography database of normal human corneas". *British Journal of Ophthalmology* 80.7 (1996): 610-616.

18. Li X., *et al*. "Keratoconus: classification scheme based on videokeratography and clinical signs". *Journal of Cataract and Refractive Surgery* 35.9 (2009): 1597-1603.

19. Nagy Kh. "New topographic classification of keratoconus". *Scientific Events Egyptian Ophthalmological Society* 2 (2009): 163-169.

20. Prakash G., *et al*. "A new, pachymetry-based approach for diagnostic cutoffs for normal, suspect and keratoconic cornea". *Eye (London)* 26.5 (2012): 650-657.

21. Probst L. "Orbscan II indicies for keratoconus". In: probst L (ed). LASIK: Advances, Controversies and custums. Thorofare. NJ: Slack, Inc (2004): 3-14.

22. Lui Z., *et al*. "Evaluation of corneal thickness and topography in normal eyes using the Orbscan corneal topography system". *British Journal of Ophthalmology* 83.7 (1999): 774-778.

23. Piven I and Barequet I. "Orbscan and Keratoconus". In: Barbara A, Rabinowitz YS (eds). Textbook on keratoconus: New insights. New Delhi: Jaypee Brothers Medical Pub 1st edition (2011): 49-57.

24. Machesney W. "Corneal topography to help detect keratoconus". *Journal of Ophthalmic Nursing and Technology* 15.5 (1996): 213-214.

25. Schlegel Z., *et al*. "Comparison of and correlation between anterior and posterior corneal elevation maps in normal eyes and keratoconus-suspect eyes". *Journal of Cataract and Refractive Surgery* 34.5 (2008): 789-795.

26. Seiler T and Quurke AW. "Iatrogenic keratectasia after LASIK in a case of Forme fruste keratoconus". *Journal of Cataract and Refractive Surgery* 24.7 (1998): 1007-1009.

27. Quisling S., *et al*. "Comparison of Pentacam and Orbscan IIz on posterior curvature topography measurements in keratoconus eyes". *Ophthalmology* 113.9 (2006): 1629-1632.

28. Nagy Kh. "Importance of corneal topography in cases of excimer laser photo-refractive keratectomy". *Bulletin of the Ophthalmological Society of Egypt* 93.1 (2000): 67-75.

29. Gatinel D. "Screening subclinical keratoconus with SCORE analyzer" (2016).

30. Chan C., *et al*. "Validation of an Objective Scoring System for forme fruste keratoconus detection and post-LASIK ectasia risk assessment in Asian eyes". *Cornea* 34.9 (2015): 996-1004.

31. IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.

32. Field A. "Discovering Statistics Using SPSS". 2nd edition. London, California, New Delhi: SAGE Publications Ltd (2006).

33. Hochberg Y and Tamhane AC. "Multiple Comparison Procedures". New York-Chichester-Brisbane-Toronto-Singapore: John Wiley and Sons (2011).

34. Belin MW. "Topography and scheimpflug imaging". Cataract and Refractive Surgery Today (2006): 48-50.

35. Arbelaez MC and Sekito MB. "Screening for subclinical keratoconus". *Oman Journal of Ophthalmology* 6.1 (2013): 1-2.

36. Schoonjans F., *et al*. "MedCalc: a new computer program for medical statistics". *Computer Methods and Programs in Biomedicine* 48.3 (1995): 257-262.

37. Miháltz K., *et al*. "Evaluation of keratometric, pachymetric, and elevation parameters of keratoconic corneas with Pentacam". *Cornea* 28.9 (2009): 976-980.

38. Wagner H., *et al*. "Collaborative Longitudinal Evaluation of Keratoconus (CLEK) study: Methods and findings to date". *Contact Lens and Anterior Eye* 30.4 (2007): 223-232.

39. Jafarinasab M., *et al*. "Sensitivity and specificity of posterior and anterior corneal elevation measured by Orbscan in diagnosis of clinical and subclinical keratoconus". *Journal of Ophthalmic and Vision Research* 10.1 (2015): 10-15.

40. Agarwal V. "Characteristics of keratoconus patients at a tertiary eye center in India". *Journal of Ophthalmic and Vision Research* 6.2 (2011): 87-91.

41. Serdarogullari H., *et al*. "Prevalence of keratoconus and subclinical keratoconus in subjects with astigmatism using pentacham derived parameters". *Journal of Ophthalmic and Vision Research* 8.3 (2013): 213-219.

42. Prakash G., *et al*. "Predictive Analysis Between Topographic, Pachymetric and Wavefront Parameters in Keratoconus, Suspects and Normal Eyes: Creating Unified Equations to Evaluate Keratoconus". *Current Eye Research* 41.3 (2016): 334-342.

43. Sonmez B., *et al*. "Identification of scanning slit-beam topographic parameters important in distinguishing normal from keratoconic corneal morphologic features". *American Journal of Ophthalmology* 143.3 (2007): 401-408.

44. Lim L., *et al*. "Evaluation of keratoconus in Asians: Role of Orbscan II and Tomey TMS-2 corneal topography". *American Journal of Ophthalmology* 143.3 (2007): 390-400.

45. Ishii R., *et al*. "Correlation of corneal elevation with severity of keratoconus by means of anterior and posterior topographic analysis". *Cornea* 31.3 (2012): 253-258.

46. Rao S., *et al*. "Role of Orbscan II in screening keratoconus suspects before refractive corneal surgery". *Ophthalmology* 109.9 (2002): 1642-1646.

47. De Sanctis U., *et al*. "Sensitivity and specificity of posterior corneal elevation measured by Pentacam in discriminating keratoconus/subclinical keratoconus". *Ophthalmology* 115.9 (2008): 1534-1539.

48. Jafarinasab M., *et al*. "Evaluation of corneal elevation in eyes with subclinical keratoconus and keratoconus using Galilei double Scheimpflug analyzer". *European Journal of Ophthalmology* 23.3 (2013): 377-384.

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