Keratoconus and Personality Traits: A Case–Control Study

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Purpose: The aim of this study was to delineate the personality traits of patients affected by keratoconus (KC) compared with a group of nonkeratoconic controls matched in age and sex.

Methods: In this prospective interventional case–control study, 60 consecutive subjects (30 KC cases and 30 healthy controls), aged 18 to 30, were enrolled at the time of their first encounter at the ophthalmology unit of the Fondazione Policlinico "Tor Vergata", Roma. After completing the ophthalmic evaluation, participants were asked to respond to the National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25). A complete psychiatric assessment was performed, including the Structured Clinical Interview for the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (SCID-5); the Symptom Check List-90-Revised (SCL-90); the Temperament Evaluation of Memphis, Pisa, Paris, and San Diego-Modified (TEMPS-M); and the NEO Five-Factor Inventory (NEO-FFI).

Results: Cases had lower quality of life than controls, as demonstrated by lower scores in all NEI VFQ-25 subdomains. Nine patients with KC (30.0%) were diagnosed by the SCID-5 with at least 1 cluster C personality disorder, resulting in a 9-fold increased risk compared with controls. Moreover, keratoconic patients showed a more pronounced psychosomatic symptomatology (SCL-90) and a characteristic neurotic temperament (TEMPS-M and NEO-FFI).

Conclusions: Our results support the hypothesis that subjects with KC feature dysfunctional coping mechanisms and personality traits, which might already be present at the first clinical encounter. Ophthalmologists should question the mental and emotional status of patients with KC and be especially careful in managing these patients.

Key Words: keratoconus, personality disorders, NEI-VFQ-25, TEMPS-M, NEO-FFI, SCL-90, SCID-5, KC

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Keratoconus (KC) is a corneal ectatic disorder featured by a progressive steepening and thinning of the cornea with consequent irregular astigmatism, responsible for the decline of visual quality and acuity.[1–4] Over the past decades, increased attention has been given to assessing patient-reported outcome measures in clinical studies.[5] For instance, results from the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) study were the first to describe patients affected by KC as having a quality of life comparable to those with moderate to severe age-related macular degeneration.[6,7] In addition to a reduced quality of life in patients with KC, a highly significant correlation was demonstrated between steeper corneas and specific domains of the National Eye Institute Visual Function Questionnaire (NEI-VFQ), such as Mental Health, Role Difficulties, and Dependency.[6,7] As per the authors' conclusions, the identified symptoms of worry, frustration, and embarrassment might be associated with depression and reduced quality of life.

The hypothesis that patients with KC present distinct personality traits is not a novelty.[8] As early as 1965, Copeman[9] reported about the relationship of KC with an *"odd mentality"*. In 1966, Ridely hypothesized that the *"compulsive scratching"* of the eye described by some patients with KC might be an outlet for *"emotional crises and upsets"*.[10] Based on this observation, in 1987, Mannis et al[11] published the first comparative study to determine whether a specific complex of personality features could be considered typical of patients with KC when compared with patients with other chronic eye diseases or subjects without visual problems. To do so, they administered to both patients and controls the Millón Clinical Multiaxial Inventory (MCMI), a standardized personality questionnaire measuring 20 personality scales. The authors observed that the data obtained by the MCMI were unable to discriminate the presence of a specific core of personality features attributable to KC, suggesting that *"interview techniques may be a necessary supplement to personality tests"*. In 1998, based on the results obtained from the Minnesota Multiphasic Personality Inventory questionnaire, Gorskova et al[12] reported patients with KC manifest a particular tendency to psychasthenia and schizophrenia.

However, in a recent review of the literature, Mannis et al[8] stated that the notion of a unique "keratoconic personality" is not demonstrable based on the available data. It is worth noting that a multimodal assessment of personality traits was performed in only 2 (13.3%) of the analyzed studies in this review.[8,13,14] In addition, a psychiatric interview was the assessment strategy only in 1 study, and it was not conducted in a structured and formalized way.[8,15]

The main aim of this study was to try to delineate the personality traits of keratoconic patients as compared with a group of age-matched and sex-matched nonkeratoconic controls at the time of the diagnosis/first clinical encounter. A multimodal approach, with the adoption of a structured interview and different psychometric scales, was the methodology we chose to explore the distinct personality domains objectively and minimize any potential risk of bias.

MATERIALS AND METHODS

Study Design and Setting

This single-center prospective interventional case––control study was conducted following the Good Clinical Practice guidelines, the tenets of the Declaration of Helsinki, and all applicable regulations. The study protocol was approved by the local institutional review board (ID: 256/21).

All examinations were performed by the same examiners using the same protocol and equipment throughout. No changes in the protocol or methods occurred after the study commencement. No power calculation analysis was performed because the methodology and the primary outcome measures of this study were not previously described in the available literature.

ELIGIBILITY CRITERIA

Participants were recruited at the ophthalmology unit of the Fondazione Policlinico "Tor Vergata" from February 2021 to November 2022, at the time of their first visit to this practice. Consecutive eligible patients were young adults aged 18 to 30 with a formal diagnosis of KC defined according to the American Academy of Ophthalmology Preferred Practice Pattern (ie, corneal topography showing a pattern consistent with KC, including inferior steepening, superior flattening, skewing of the radial axes, and K2 ≥46.0D diopters (D), along with corneal thinning located in the context of the apex of the conus).[16] Age-matched and sex-matched healthy control subjects were enrolled if only affected by mild refractive disorders (ie, spherical equivalent refraction of −4.00 to +2.00 D, astigmatism of 2.50 D or less, anisometropia of 1.50 D or less, and corrected distance visual acuity (CDVA) of 0.0 logarithm of the minimum angle of resolution or more (Snellen equivalent, 1.0 or 20/20 in either eye)).

Exclusion criteria were the presence of (1) actual or past non-KC ocular disease in both eyes, such as cataracts, intraocular lens implants, macular disease, and optic nerve disease (eg, glaucoma, optic neuritis, or optic atrophy), and/or (2) cognitive impairment or any other known psychiatric disorder. We also excluded subjects if investigators believed they had contraindications that made them unsuitable for participation (eg, severe motor or auditory impairment). Written informed consent was obtained from all subjects before participation.

Ophthalmological Assessment

On enrollment in the study, demographic data and a detailed ocular and systemic history were recalled for each patient, including the presence of systemic comorbidities (ie, atopia, asthma, allergic rhinitis, and obstructive sleep apnea), the use of rigid gas-permeable contact lenses (GP-SCLs), and previous intervention(s) (eg, keratoplasty and cross linking (CXL)). In addition, baseline clinical data were retrieved, such as weight, height, and body mass index (BMI).

Uncorrected (UDVA) and corrected distance visual acuity (CDVA) were measured using high-contrast Bailey–Lovie charts, using the Early Treatment Diabetic Retinopathy Study protocol.[17] Keratometry of the central 3 mm of the anterior corneal surface (ie, K1 and K2) and minimum corneal thickness were recorded for each eye using Placid disk-based topography (Atlas 9000, Zeiss, Inc, Thornwood, NY) and anterior segment optical coherence tomography (VISANTE, Zeiss, Inc, Thornwood, NY). All patients were screened for the presence of lax eyelid condition and underwent a dilated fundus slit-lamp examination to exclude the presence of lens, vitreous, macular, and/or optic nerve disorders.[18]

At baseline, each subject was also asked to complete the NEI-VFQ. The NEI-VFQ is a vision-related quality of life instrument designed to assess patients' perception of visual function and quality of life.[19] The base questionnaire includes 25 items that comprise 11 subscales exploring general health and vision, ocular pain, near and distance activities, driving, color vision, and peripheral vision. The relationship between 4 components of psychological well-being (ie, social function, mental health, role difficulties, and dependency) and vision is also evaluated. NEI VFQ scores range from 0 to 100, with a higher score representing better functioning.

Psychiatric Assessment

Included subjects were subsequently asked to complete a structured interview and 3 self-rating questionnaires. The interviews were conducted in compliance with the Structured Clinical Interview for the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (SCID-5-CV and SCID-5-PD).[20] The physicians conducting the interviews were blinded to the clinical status (KC vs. non-KC) of the individuals under evaluation. The 3 questionnaires, whose Italian version has been already validated, were the Temperament Evaluation of Memphis, Pisa, Paris, and San Diego-Modified (TEMPS-M) scale;[21] the NEO Five-Factor Inventory (NEO-FFI);[22] and the Symptom Check List-90 Revised (SCL-90 R).[23]

Structured Clinical Interview for the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*

The SCID-5 was conducted in compliance with the SCID-5-Clinical Version (SCID-5-CV) and SCID-5-Personality Disorder (SCID-5-PD), which were sequentially administered. The SCID-5-CV is the gold-standard semistructured diagnostic interview for making DSM-5 diagnosis, designed to improve the reliability of the psychiatric diagnostic assessment process.[24] It is organized into diagnostic modules, including mood disorders, psychotic disorders, substance use disorders, anxiety disorders, obsessive–compulsive and related disorders, eating disorders, somatic symptom disorders, some sleep disorders (ie, insomnia and hypersomnolence disorders), "externalizing disorders" (ie, intermittent explosive disorder, gambling disorder, and adult attention deficit hyperactivity disorder), and trauma and stressor-related disorders.[20]

The SCID-5-PD is a semistructured diagnostic interview to assess the presence of DSM-5 personality disorders. It consists of 2 parts a short, self-administered questionnaire with a yes/no dichotomous answer (SCID 5-SPQ), followed by a semistructured interview for an in-depth analysis of any items on the questionnaire that were answered affirmatively. This approach allows the clinician to describe the presence of eventual personality disorders both categorically (ie, yes or no) and dimensionally (eg, cluster A, B, and C).[20,24] The interview execution time was variable, ranging from 10 minutes to 1 hour.

Temperament Evaluation of Memphis, Pisa, Paris, and San Diego-Modified

Temperament refers to a genetically determined emotional reactivity to the environment, which—in combination with life experiences—leads to the development of personality traits.[25] Based on the Kraepelin theory of the fundamental states of personality, the TEMPS-M is a self-rating 35-item questionnaire assessing 5 temperaments (ie, depressive, hyperthymic, irritable, cyclothymic, and anxious) with a 5-point Likert scale ranging from "not at all" to "very much".[21,26] Specifically, I) cyclothymic temperament refers to chronic cycling of mood polarities with unstable self-esteem and energy, II) irritable temperament is characterized by irritable behaviors, III) hyperthymic temperament by increased levels of energy and optimism, IV) depressive temperament is characterized by low levels of energy and introversion, and V) anxious temperament defined by the chronic disposition to worry (worrying attitudes).[27] The duration of the questionnaire administration was approximately 10 to 15 minutes.

NEO Five-Factor Inventory

The NEO-FFI, a short form of the NEO Personality Inventory-Revised (NEO-PI-R), contains 60 self-reported items, equally distributed among the 5 factors of the 5-factor model of personality: neuroticism (N), in which high scores are associated with emotional dysregulation and low scores with emotional blandness; extraversion (E), in which high scores indicate dominating social interactions and low scores indicate social isolation; openness to experience (O), in which high scores indicate eccentric or nonconformist thinking and low scores suggest a constricted range of interests; agreeableness (A), in which high scores indicate need to please others and passivity and low scores indicate quarrelsomeness and cynicism; and conscientiousness (C), in which high scores indicate compulsivity and low scores indicate aimlessness. Items are answered on a 5-point Likert scale ranging from "certainly disagree" to "certainly agree". Showing an inevitable theoretical overlap, the NEO-FFI has been proposed as a helpful instrument for external validation of the TEMPS-M scale.[28] The test execution time was approximately 15–20 minutes.

Symptom Check List-90 Revised

The SCL-90-R is a self-rating 90-item multidimensional questionnaire designed to screen for a broad range of psychological symptoms.[29,30] The 90 items are rated on a 5-point Likert scale ranging from "not at all" to "extremely". The answers are combined in 9 primary symptom dimensions: somatization, obsessive–compulsive, interpersonal sensitivity, depression, anxiety, anger, hostility, phobic, anxiety, paranoid ideation, and psychoticism. Three global indices evaluate different aspects of the experienced psychological distress: I) the Global Severity Index (GSI) is a generalized measure of global psychological distress; II) the Positive Symptom Total (PST) is the aggregate measure of all self-reported symptoms; and III) the Positive Symptom Distress Index (PSDI) is an indicator of the mean symptom intensity.[29,30] The total duration of the questionnaire administration was approximately 15 to 20 minutes.

Statistical Analysis

All results were expressed as mean (standard deviation) and count (percentage) in the presence of continuous and categorical variables, respectively. For the study and control groups, ocular data were reported regarding the eye with the steepest meridian (K2).

NEI VFQ-25, SCL-90, TEMPS-M, and NEO-FFI data were scored according to the developers' guidelines, with no imputation conducted for missing values. NEI VFQ-25 test results were reported with data from both CLEK study[6] and from a population of age-matched, nonkeratoconic rigid contact lens wearers as references.[31] SCL-90 and NEO-FFI test results were expressed as T-score (SD), assuming a normative mean of 50 and a standard deviation (SD) of 10. TEMPS-M scores were expressed as mean (SD) and compared with an age-matched European reference population.[26]

The Student t test was performed to compare parametric, unmatched, continuous variables. The Kruskal–Wallis test was used to compare nonparametric, unmatched, continuous variables. The Pearson χ^2 test was performed in the presence of categorical variables, adjusting for multiple comparisons using the conservative Bonferroni–Holm method. P values of <0.05 were considered statistically significant for all analyses.

Internal consistency reliability of psychometric tests (ie, NEI VFQ-25, TEMPS-M, NEO-FFI, SCL-90) was assessed using Cronbach coefficient alpha to determine the extent to which individual items within each scale are related to each other and with the scale as a whole. Values range on an interval level scale from 0 to 1.0, with higher scores indicating a more reliable (homogeneous) instrument. Specifically, coefficients >0.9 indicate high reliability suitable for evaluations of individual patients, and those between 0.7 and 0.9 indicate good internal consistency suitable for group comparisons. IBM SPSS Statistics for Macintosh (v. 28.0.0.0 (190)) was used for the analysis.

RESULTS

Per the study protocol, 60 White patients were included in the study, 30 in the KC and 30 in the control groups. Overall, no substantial demographic and/or clinical features emerged between the 2 groups, as reported in Table 1.

Statistically significant differences emerged from the comparison of weight and BMI, which were higher in the study group than in controls (weight: $P = 0.0200$; BMI: $P = 0.0047$). As expected, KC eyes presented steeper and thinner corneas, as well as worse UDVA and CDVA than healthy controls.

In the KC group, 19 of the 30 patients (63.3%) reported a history of eye rubbing, whereas 9 of the 30 subjects (30%) were GP-RCL users. One (3.3%) of the included KC eyes presented a history of corneal transplant (1 deep anterior lamellar keratoplasty).

National Eye Institute Visual Function Questionnaire-25 Scale

Mean scores for the NEI VFQ-25 are reported in Supplementary Table 1 (http://links.lww.com/ICO/B537). KC-affected patients scored significantly lower (ie, worse visual function) in all NEI VFQ-25 subscales compared with the control group and a reference group of rigid contact lens wearers of similar age.[31] However, all scale scores in the KC group were similar to those of patients with KC in the CLEK study.[6]

Two scales in the KC group had scores over 90: dependency and color vision. Ocular pain, near activities, social function, and peripheral vision had scores of 81.2, 82.9, 88.5, and 81.2, respectively.

The internal consistency of the NEI VFQ-25 in this sample was good (Supplementary Table 1, http://links.lww.com/ICO/B537). The overall Cronbach alpha statistic was 0.926, and all multiitem scales except ocular pain and driving reported a Cronbach alpha above 0.7 (Cronbach alpha 0.613 and 0.584, respectively) (Supplementary Table 1, http://links.lww.com/ICO/B537).

Structured Clinical Interview for the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*

As expressed in Table 2, the SCID-5-CV results demonstrated that patients with KC are more prone to mood and anxiety disorders than non-KC controls. However, this difference did not achieve statistical significance.

According to the SCID-5-PD, 2 and 3 patients with KC and none of the controls qualified for cluster A and cluster B personality disorders, with no significant difference between the 2 groups ($P = 0.150$ and $P = 0.076$, respectively). However, 9 of the 30 (30.0%) KC-affected subjects and 1 of the 30 controls (3.3%) were classified as presenting at least 1 cluster C personality disorder (RR: 9.0, 95% CI: 1.6–53.4; $P = 0.006$). Among the patients with KC qualifying for cluster C, 8 of 9 (88.9%) and 1 of 9 (11.1%) were defined as presenting an obsessive–compulsive personality disorder and an avoidant personality disorder, respectively.

Temperament Evaluation of Memphis, Pisa, Paris, and San Diego Scale

Table 3 reports the relevant results of the TEMPS-M scale. Affective temperament scores showed disease-specific differences. Keratoconic patients presented significantly higher scores on depressive, cyclothymic, and irritable temperament scales than the control group and a reference group of age-matched European subjects.[26]

The Cronbach alpha for each scale was calculated to assess reliability. Alpha scores varied between 0.692 (cyclothymic temperament) and 0.787 (hyperthymic temperament), with a global Cronbach alpha statistic of 0.732.

TABLE 1. Demographic and Clinical Features of the Study and Control Groups

Demographic and Clinical Features			
	KC (*n* = 30)	Control (*n* = 30)	*P*
Age	23.8 ± 2.9	23.8 ± 2.8	0.9767
Sex [female]	11/30 (36.7%)	13/30 (43.3%)	0.7925
Weight [Kg]	77.5 ± 21.1	66.5 ± 12.9	**0.0200**
Height [cm]	173.6 ± 6.62	173.4 ± 8.23	0.9381
BMI [Kg/m²]	25.6 ± 6.4	21.9 ± 2.7	**0.0047**
Systemic comorbidities [atopia, asthma, allergic rhinitis, or obstructive sleep apnea]	4/30 (13.3%)	1/30 (3.3%)	0.3533
Lax eyelid condition	0/30 (0%)	0/30 (0%)	>0.9999
K1	44.4 ± 2.8	42.9 ± 1.3	**0.0115**
K2	47.8 ± 3.6	44.2 ± 1.4	**< 0.0001**
MCT (μm)	486.6 ± 45.9	532.3 ± 32.3	**< 0.0001**
UDVA	0.5 ± 0.3	0.2 ± 0.2	**< 0.0001**
CDVA	0.2 ± 0.3	0.00 ± 0.00	**< 0.0001**
Family history of KC	8/30 (26.7%)	0/30 (0%)	**< 0.0001**
Eye rubbing	19/30 (63.3%)	0/30 (0%)	**< 0.0001**
CXL	13/30 (43.3%)	0/30 (0%)	
GP-RCL	9/30 (10%)	0/30 (0%)	
Transplant history	1/30 (3.3%)	0/30 (0%)	

Results are expressed as mean ± standard deviation or as count (percentage). Abbreviations. KC: keratoconus; BMI: body mass index; MCT: minimum corneal thickness; UDVA: uncorrected distance visual acuity; CDVA: corrected distance visual acuity; CXL: corneal cross-linking; GP-RCL: gas-permeable rigid contact lenses.

TABLE 2. Quick-SCID and SCID-Personality Disorder Results in the Study and the Control Groups

Structured Clinical Interview for the *Diagnostic and Statistical Manual of Mental Disorders*				
Scale	KC	Control	Risk ratio	*P*
Q-SCID				
Mood disorder	9/30 (30.0%)	4/30 (13.3%)	2.3 (0.8–6.4)	0.1172
Anxiety disorder	5/30 (16.7%)	4/30 (13.3%)	1.3 (0.4–3.9)	0.7177
Psychotic disorder	0/30 (0.0%)	0/30 (0.0%)	NA	NA
Others	2/30 (6.7%)	2/30 (6.7%)	1 (0.2–5.4)	>0.9999
SCID-PD				
Cluster A	2/30 (6.7%)	0/30 (0.0%)	NA	0.1503
Cluster B	3/30 (10.0%)	0/30 (0.0%)	NA	0.0756
Cluster C	9/30 (30%)	1/30 (3.3%)	9.0 (1.6–53.4)	**0.0056**
Others	0/30 (0.0%)	0/30 (0.0%)	NA	NA

Results are expressed as counts and percentages, whereas the risk ratio values are expressed with their 95 confidence intervals in brackets. Abbreviations. KC: keratoconus; Q-SCID: quick-SCID; SCID-PD: SCID-Personality Disorder.

NEO Five-Factor Inventory Scale Results

The NEO-FFI test results are reported in Table 4. Overall, patients with KC scored significantly higher on the neuroticism scale than the control group. No other differences were found between groups after statistical analysis.

Both groups scored low on the extroversion, openness, agreeableness, and conscientiousness scale. The global Cronbach alpha was 0.819. All scales were highly reliable, with neuroticism and conscientiousness being particularly so.

Symptoms Check List-90 Scale

Results from the SCL-90-R are reported in Table 5. GSI ($P = 0.025$), PST ($P = 0.006$), and PSDI (0.021) were higher in KC than in non-KC subjects. Subscale parameter scores for somatization, obsessive–compulsive, interpersonal sensitivity, hostility, and psychoticism were also significantly higher in patients with KC. No other significant differences were identified, although all scores were higher in patients with KC than in controls (Table 5).

The global Cronbach alpha was 0.945. All scales were highly reliable, with an alpha score >0.90.

DISCUSSION

The main aim of the present work was to delineate the personality traits of consecutive KC-affected patients versus non-KC healthy controls at the time of their first encounter at our institution. This aim mainly originates from the observation of the CLEK study, which reported people with KC as scoring low in the NEI VFQ-25 subscales of mental health, role difficulties, and dependency.[6]

In our cohort, including an equal number (ie, 30) of age-matched and sex-matched subjects with KC and non-KC subjects, mean weight and BMI were higher in the study than in the control group ($P = 0.0200$ and $P = 0.0047$). In addition, excessive eye rubbing was reported by a higher percentage of KC-affected patients than by healthy subjects ($P < 0.0001$) (Table 1).

Furthermore, NEI VFQ-25 subscale scores seemed significantly lower in patients with KC than in controls and in a previously described group of non-keratoconic GP-RCL wearer subjects.[31] This finding suggests that the vision-related quality of life in patients with KC was significantly affected by the ocular disease (Supplementary Table 1, http://links.lww.com/ICO/B537).[31] This evidence, in line with the results of the CLEK study, mainly differs from the latter for the higher scores we retrieved in the ocular pain domain in subjects with KC.[6,7] This discrepancy might be attributable to the lower number of cornea-transplanted eyes in our cohort (3.3 vs. 10.0%). In fact, keratoplasty has been reported to significantly affect the pain subscale domain of the NEI VFQ-25 in patients with KC.[32]

In addition, results from psychiatric questionnaires indicated that keratoconic patients experience significant overall psychological distress, as indicated by the 3 global indices of the SCL-90 (ie, GSI, PST, and PSDI) (Table 5). A neurotic temperament profile of patients with KC clearly emerged (ie, NEO-FFI), where somatization, obsessive–compulsive, psychoticism traits, and marked interpersonal sensitivity constitute the core of the psychosomatic symptomatology (ie, SCL-90). Interestingly, Blöink et al reported a strong positive correlation between the neuroticism temperament of the NEO-FFI and the depressive, cyclothymic, and irritable subscales of the TEMPS-M, evidence which further corroborates our findings (Tables 3 and 4).[28]

According to the SCID-PD, the gold-standard semi-structured diagnostic interview for personality disorders, 9 of the 30 patients with KC (30.0%) were diagnosed with at least 1 cluster C personality disorder, with a 9-fold increased risk as compared with the control group (Table 2). The obsessive–compulsive personality disorder was the most commonly encountered cluster C personality disorder.

TABLE 3. TEMPS-M Results in the Study and the Control Groups Compared With a Reference Group of Subjects of Similar Age

Temperament Evaluation of Memphis, Pisa, Paris, and San Diego Test Results					
TEMPS-M scale	KC *mean (SD)*	Control *mean (SD)*	*P*	Cronbach alpha[§]	German norm population[24] *mean (SD)*
Depressive	18.9 (7.2)	14.9 (6.2)	**0.0358**	0.713	14.7 (5.8)
Cyclothymic	19.9 (8.4)	12.6 (5.2)	**0.0003**	0.692	15.7 (5.2)
Hyperthymic	21.7 (4.8)	22.1 (4.9)	0.7684	0.787	20.6 (4.6)
Irritable	14.8 (6.6)	11.8 (3.6)	0.0359	0.734	15.7 (4.9)
Anxious	15.8 (7.2)	13.9 (5.5)	0.3089	0.756	14.7 (4.9)

§For this study sample only.
KC: keratoconus.

TABLE 4. NEO-FFI Results in the Study and the Control Groups

NEO Five-Factor Inventory Scale Results				
NEO-FFI scale	KC *mean (SD)*	Control *mean (SD)*	*P*	Cronbach alpha§
Neuroticism	62.1 (8.7)	53.2 (7.0)	**0.0007**	0.839
Extroversion	42.0 (6.9)	45.5 (10.3)	0.9563	0.782
Openness	41.0 (7.4)	41.4 (5.6)	0.5872	0.731
Agreeableness	37.9 (9.4)	36.0 (7.9)	0.5620	0.752
Conscientiousness	37.3 (6.6)	38.4 (5.9)	0.8608	0.803

§For this study sample only.
Results are expressed as T-score. Abbreviations. KC: keratoconus.

Several observations might explain the occurrence of dysfunctional personality traits in KC. For instance, the onset of KC typically occurs at a young age (eg, young adults between the ages of 12 and 30), during 1 of the most important phases of the individual's psychosocial and occupational development.[33,34] The associated visual difficulties, the awareness of being affected by a disorder requiring periodic medical visits, and the need to undergo both noninvasive and invasive treatments (eg, use of spectacles or contact lenses, cross-linking, and keratoplasty) are some of the elements which may act as a trigger for the development of dysfunctional personality traits and pathological coping mechanisms.[3,4,8,32–35]

In this regard, it has been widely described that eye rubbing is considered a significant risk factor for KC.[36,37] This behavior may be linked to the externalization of emotional stress accumulated in adolescence or as a compulsion toward pervasive ideas.[10,38,39] Interestingly, both body weight and BMI levels were significantly higher in the study group than in the control group (Table 2). The coexistence of food overconsumption and excessive eye rubbing in the KC arm may represent a compulsive outlet for strong negative emotional thoughts in these patients.[40,41]

Furthermore, although previously believed to be a noninflammatory condition, a growing body of evidence suggests that aberrant activation of local and/or systemic proinflammatory pathways is one of the mechanisms responsible for the development and progression of the ectatic damage in KC.[42–44] For instance, Loh et al recently described the corneal expression pattern of 120 cytokines involved in wound healing, neuroprotection, angiogenesis, and inflammation. Twenty-three of these mediators were significantly overexpressed in KC corneal buttons compared with non-KC samples, with 15 detectable in keratoconic corneas only.[44] Interestingly, an upregulation of similar proinflammatory mediators (eg, IL-1, IL-6, and IL-12) has been widely described in the serum samples of patients with various dysfunctional personality traits and temperaments, including obsessive–compulsive personality disorder and neuroticism, respectively.[45–47] As such, it is possible to hypothesize that a genetic/epigenetic background favorable to developing a systemic proinflammatory cytokine milieu is responsible for overlapping dysfunctional personality traits and KC in the same patient.

Although the evidence to support a causal relationship between each of these elements is far from conclusive, our data underline the urgency of providing medical care to patients with KC that does not end with the management of the ocular disease alone. In fact, the high levels of psychological distress typical of patients with KC may exert a predominant effect on the quality of life and significantly affect the social and working spheres.

The strengths of our study include the consecutive enrollment criteria, the presence of age-matched and sex-matched controlled group, and the use of a multimodal and standardized psychiatric assessment approach (3 self-rating questionnaires and 2 semistructured interviews). Limitations of the study include the case–control design because we did not analyze the evolution of personality disturbances over time. In this regard, it must be acknowledged that this study aims to evaluate the presence of specific personality traits in keratoconic patients at the time of the diagnosis/first encounter, not the evolution of eventual psychological dysfunctions. Second, our findings may not be generalizable to the entire KC population because (a) the patients included in this study are in their young adulthood and (b) the entire cohort extracted is from a single tertiary health care center. In addition, even if negligible, a subgroup of patients (ie, 2) was excluded from the study for refusal to participate. Furthermore, as the methodology and primary outcome measures

TABLE 5. SCL-90 Results in the Study and the Control Groups

Symptom Check List 90 Test Results				
SCL-90 scale	KC mean (SD)	Control mean (SD)	*P*	Chronbach's alpha
Somatization	55.0 (11.1)	48.5 (8.1)	**0.0221**	0.944
Obsessive–compulsive	60.9 (12.5)	52.1 (9.9)	**0.0081**	0.938
Interpersonal sensitivity	57.1 (14.1)	47.3 (9.2)	**0.0046**	0.937
Depression	51.1 (14.5)	47.6 (9.3)	0.3042	0.937
Anxiety	54.8 (16.3)	47.6 (10.7)	0.0645	0.949
Hostility	50.9 (15.5)	46.8 (9.8)	**0.0389**	0.947
Phobic	46.2 (15.3)	42.3 (10.2)	0.2930	0.944
Paranoid ideation	54.2 (16.7)	48.4 (10.6)	0.1387	0.940
Psychoticism	54.8 (16.0)	45.5 (12.3)	**0.0259**	0.937
GSI	54.2 (15.2)	47.9 (10.0)	**0.0254**	0.937
PST	57.3 (13.0)	47.9 (9.6)	**0.0061**	0.937
PSDI	51.4 (14.3)	43.9 (7.5)	**0.0213**	0.940

Results are expressed as T-score. Abbreviations. KC: keratoconus; GSI: Global Severity Index; PST: Positive Symptom Total; PSDI: Positive Symptom Distress Index.

applied in this study were not previously described in the available literature in the context of KC, no power calculation analysis was performed. Along the same lines, it is worth noting that setting the probability of the type I error to <0.01 would have not affected the significance of our results, but it would have underpowered the study.[48]

Despite these limitations, this study is the first to describe subjects with KC having a specific neurotic temperament and a higher risk for dysfunctional cluster C personality disorders at the time of the diagnosis/first encounter. As reported by the authors of the CLEK study, KC is "a disease of relatively low prevalence that rarely results in blindness, but because it affects young adults, the magnitude of its public health impact is disproportionate to its prevalence and clinical severity".[6] Our findings suggest that this burden might be mediated not only by the ocular disease per se but also by the psychological disturbances these patients experience. Accordingly, ophthalmologists should be encouraged to question patients with KC about their mental and emotional status. This may result in early detection of those subjects needing specific psychiatric consultation and psychological support.

Further research is needed to understand the temporal relationship between KC and dysfunctional personality traits and the causal relationship between them. Identifying risk factors and biophysical markers of a diagnostic and prognostic nature would exponentially enrich our understanding and knowledge of pathologies, which, although very different, could represent different facets of a single, broad pathological spectrum.

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