



Psychiatric morbidity of patients with keratoconus: A cross-sectional study

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ABSTRACT

Background: This study aimed to determine the prevalence of psychiatric disorders in patients with keratoconus and the effect of clinical parameters and psychiatric morbidity on quality of life in this patient group.

Materials and methods: This cross-sectional study enrolled 94 patients with keratoconus. All patients underwent a complete ophthalmic and psychiatric examination and completed the The National Eye Institute Refractive Error Quality of Life Instrument-42 (NEI-RQL-42), Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) questionnaires. The current diagnosis of psychiatric disorders was determined using the Structured Clinical Interview for DSM-IV (SCID). The impact of disease severity (binocular BCVA ≥ 0.4 logMAR, steep K reading ≥ 52 , and Amsler-Krumeich grades) on vision-related quality of life was also analyzed.

Results: The patients' mean age was 23.9 ± 4.8 (range, 18–40) years. Of the 94 participants 35 (37.2%) had a psychiatric diagnosis, 13 (13.8%) had moderate-severe depression and 20 (21.2%) had moderate-severe anxiety according to the BDI and BAI, respectively. The probability of having a psychiatric disorder was higher if the keratoconus was more severe. Patients with a psychiatric diagnosis scored lower on physical functioning, role limitations due to emotional problems, energy/fatigue; emotional well-being, social functioning and pain subscales of the Short Form-36 (SF-36). Having a SCID-1 psychiatric diagnosis and the presence of a psychiatric disorder did not significantly affect NEI-RQL-42 questionnaire scores.

Conclusions: There was high psychiatric morbidity among patients with keratoconus. Having a psychiatric disorder was associated with lower QoL as measured using the SF-36.

1. Introduction

Keratoconus is an asymmetric, progressive, and noninflammatory disease of the cornea associated with visual impairment and asymmetric astigmatism. It typically presents in adolescence and progresses until the third or fourth decade of life. A recent meta-analysis performed on over 7 million patients from 15 different countries reported a global prevalence of 138/100,000 [1]. Although optical rehabilitation can be provided by glasses, contact lenses, and intrastromal rings, corneal cross-linking is the only treatment option to halt or at least slow the progression of the disease [2].

Although keratoconus is a rare disease, it can cause serious

emotional and psychosocial difficulties in patients. Adolescence and early adulthood are periods in which young people develop physically, cognitively, and psychosocially, looking for self-identity and making plans for the future [3]. Therefore, a chronic disease that develops in this period and has a progressive course may have an impact on the individual's psychosocial life. Specifically, the disease may have negative effects on patients' daily life, work life, and psychosocial development due to progressive vision loss [4].

Keratometric readings and visual acuity are objective methods used to evaluate the clinical status of patients with keratoconus. However, its effects on quality of life (QoL) and functioning in everyday life are ignored during routine clinical interviews. Studies have shown that the

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QoL of patients with keratoconus is impaired in relation to their vision loss [5,6]. As a part of the Collaborative Longitudinal Evaluation of Keratoconus Study, vision-related QoL (VRQoL) of patients with keratoconus, as measured using the National Eye Institute Vision Function Questionnaire-25 (NEI-VFQ-25), was evaluated in these studies. VRQoL was significantly impaired in patients with keratoconus. Despite relatively good visual acuity (VA) (95% of patients with VA over 20/40), patients with keratoconus reported VRQoL scores similar to those of patients with moderate-to-severe age-related macular degeneration. The factors most closely associated with poor VRQoL were poor VA (<20/40) and steep corneal curvature (>52D) [7]. A number of VRQoL questionnaires have been developed for ocular diseases. Among these is the National Eye Institute Refractive Error Quality of Life (NEI-RQL-42), which is a disease-specific questionnaire designed to assess the impact of refractive error and its correction on vision-related functioning.

Some studies have focused on the personality characteristics of patients with keratoconus, showing that they have different personality traits, such as paranoia, skepticism, anxiety, compulsivity, dependence, hyperactivity, and insecure personality traits [8,9], but other studies have found different results [10,11]. A recent review reported that there was no personality structure unique to keratoconus [12]. Giedd et al. [13] showed that such patients used maladaptive coping mechanisms and that they were less respectful, conforming, and cooperative in the interaction with their physicians. In addition, there are also anecdotal case reports describing keratoconus with comorbid psychiatric disorders such as schizophrenia and obsessive-compulsive disorder [14,15]. In a preliminary report, as a result of psychiatric interviews, Besancon et al. demonstrated a higher incidence of psychosomatic traits in 34 patients with keratoconus [16]. In a study investigating the prevalence of depression in eye diseases, keratoconus was not significantly associated with increased depression scores [17].

Despite these different studies on personality and anecdotal case reports, to the best of our knowledge, no study has investigated the morbidity of psychiatric disorders in this patient group. Accordingly, we aimed to evaluate the psychiatric morbidity of patients with keratoconus through structured psychiatric interviews. We also aimed to examine the impact of psychiatric disorders on the QoL of these patients.

2. Methods

Patients with a diagnosis of keratoconus were enrolled in this cross-sectional study at Marmara University Department of Ophthalmology and Department of Psychiatry. The study sample consisted of 94 patients aged 18 years and over who presented to the ophthalmology outpatient clinic with a diagnosis of keratoconus. The inclusion criteria were as follows: (1) a diagnosis of keratoconus, (2) previous corneal cross-linking at least 6 months ago, (3) age between 18 and 65 years, and (4) the ability to sufficiently read, write, and comprehend the Turkish language. Mental retardation and psychotic exacerbation were reasons for exclusion from the study. Patients were also excluded if other ocular diseases in addition to keratoconus were diagnosed. We evaluated 156 consecutively admitted patients during the study period. From the patient sample, 27 patients were excluded due to the time criterion concerning cross-linking, and the remaining 33 refused to participate in the study. After applying the inclusion and exclusion criteria, 94 patients were eligible for the present study.

The diagnosis of keratoconus should involve medical history, refraction, keratometry, corneal topography, and slit-lamp examination. Astigmatism >5 diopters (D) and/or keratometry values (K1/K2) > 48 D, maximum keratometry (Kmax) reading >49 D, central corneal thickness (CCT) <470 mm, and corneal asphericity >0.50 mm are the topographic parameters that raise suspicion for keratoconus. [18,19].

All participants underwent detailed ophthalmologic examinations, which included uncorrected (UDVA) and corrected (CDVA) distance visual acuity in logMAR units and refractive errors (spherical equivalent and astigmatism and keratometric indices [flat (K1), steep (K2), mean

(Kmean), and maximum (Kmax)] measured using corneal tomography (Pentacam; Oculus Optikgeräte GmbH, Wetzlar, Germany) in the most affected eye. Binocular best corrected visual acuity (binocular CDVA, logMAR) was also recorded. Patients with keratoconus were classified using the Amsler-Krumeich classification (Krumeich 1998), based on mean K-readings on the anterior curvature sagittal map, thickness at the thinnest location, and the refractive error of the patient. The impact of the disease severity (binocular CDVA ≥ 0.4 logMAR, steep K reading ≥ 52 diopters (D) and Amsler-Krumeich grades) on VRQoL was also analyzed. The NEI RQL-42 was administered to all patients.

2.1. National Eye Institute refractive error quality of life

The NEI-RQL-42 is a commonly used questionnaire that seeks to measure refractive error-related QoL [20]. The assessment of refractive error-related QoL is an important outcome measure for the assessment of many refractive surgery procedures. The scored questionnaire consists of 42 items (questions) across 13 subscales, including clarity of vision, expectations, near vision, far vision, diurnal fluctuations, activity limitations, glare, symptoms, dependence on correction, worry, suboptimal correction, appearance, and satisfaction with correction. The answers for each question are evaluated between 0 and 100 points. Positive answers are given higher scores, and negative answers are given lower scores. High scores are an indicator of good QoL. The Turkish version of the NEI-RQL-42 was established by Toker et al. [21]

After detailed examinations of patients with keratoconus by the Ophthalmology Department, patients who agreed to participate in the study were referred to the Psychiatry Outpatient Clinic. In the Psychiatry Department, after obtaining sociodemographic data of the individuals, the Structured Clinical Interview (SCID-I) for DSM-IV Axis I Disorders was performed, and the Beck Anxiety Inventory (BAI) and SF-36 Quality of Life Scale were given to all participants.

The study was approved by the Clinical Research Ethics Committee and was performed in accordance with the criteria of the Declaration of Helsinki. Informed consent was obtained from all participants before the study.

2.2. Psychiatric evaluation

Age, sex, marital status, level of education, comorbid medical disorders, history of psychiatric disorders, substance use history and other sociodemographic variables were collected. Participants' psychiatric diagnosis was made through a semistructured interview using SCID-I by a single trained psychiatrist (MY). The depression and anxiety levels of the participants were measured using the Beck Depression Inventory [(BDI) 0–9 = minimal depression, 10–18 = mild depression, 19–29 = moderate depression, and 30–63 = severe depression] and the BAI (0–7 = minimal anxiety, 8–15 = mild anxiety, 16–25 = moderate anxiety, and 26–63 = severe anxiety), respectively. Health-related functioning of the participants was measured using the 36-item Short Form (SF-36) health survey.

2.3. Statistical analysis

For the statistical analysis of the data, SPSS for Windows version 21.0 (SPSS Inc., Chicago, Illinois, USA) software was used. The normality of the distribution of the variables was evaluated using the Kolmogorov-Smirnov test. Descriptive statistics for all sociodemographic and other variables were calculated and expressed as appropriate frequencies, mean values, and standard deviations. Only one eye (the most affected eye) of each study participant was included in the statistical analysis. The severity of the disease (binocular CDVA ≥ 0.4 logMAR, steep K reading ≥ 52 diopters (D) and Amsler-Krumeich grade) was categorized for the statistical analysis. These severity parameters were compared with and without a psychiatric diagnosis according to SCID-I in patients with keratoconus using the chi-square test. SF-36 scores were compared

with and without a psychiatric diagnosis according to SCID-1 in patients with keratoconus using the Mann-Whitney *U* test. Spearman's correlation test was used to examine the relationship between the NEI-RQL total score and SF-36 subscale scores. Multivariate linear regression analysis was used to evaluate the association between the mean NEI-RQL-42 subscales and the severity of keratoconus disease indicators. A *p*-value less than 0.05 was considered statistically significant.

A priori power analysis was conducted by using data from Aydin Kurna and colleagues [22] and Moschos and colleagues [23] data. Aydin and colleagues reported the QoL of grade I (*n* = 6) and IV (*n* = 6) patients with keratokonon as 82.6 ± 12.7 and 67.8 ± 25.1; respectively (i.e. an effect size of 0.7). With an a priori power analysis for *t*-test for independent groups at an alpha level of 0.05 and 95% power, we would require 110 patients with keratokonon while 80 patients led to 87.0% power [24]. As for the effects of psychopathology the effect size for depression symptoms in keratokonon as reported by Moscho and colleagues [23] was large (i.e. Cohen's *d* = 1.1) and we would require only 13 patients with keratokonon to determine such an effect size [24]. In the end, we enrolled 94 patients.

3. Results

The sample consisted of 94 patients with keratoconus (40 females, 42.6%). The mean age of the patients was 23.9 ± 4.8 (range, 18–40) years. Demographic variables, visual acuities (UDVA, CDVA, and binocular CDVA), refractive errors, and keratometric readings (K1, K2, Kmean, and Kmax) in the most (more severely) affected eye are given in Table 1.

Patients were graded according to the Amsler-Krumeich keratoconus

Table 1
Sociodemographic and clinical variables of patients with keratoconus.

Variables	Mean ± SD or percentage
Age	23.9 ± 4.8
Sex (female, n, %)	40 (42.6)
Years in education	
Marital status (married, n, %)	39 (41.5)
Employment status (regular, %)	43 (45.7)
SES (normal)	59 (62.8)
Comorbid medical disorder (Present, %)	19 (20.2)
Family history of psychiatric disorder (Present, %)	18 (19.1)
Past history of psychiatric disorder (Present, n, %)	43 (45.7)
Smoking (Yes, %)	32 (34.0)
Spheric diopter	-4.2 ± 3.6
Astigmatic diopter	-4.7 ± 2.9
Spheric equivalent	-6.3 ± 4.6
UDVA (logMAR)	0.5 ± 0.3
CDVA (logMAR)	0.4 ± 0.3
K1	46.3 ± 4.3
K2	50.2 ± 4.8
K _{mean}	48.3 ± 4.4
Thinnest pachymetry (µm)	443.7 ± 40.2
K _{max}	58.3 ± 7.4
Binocular vision	0.31 ± 0.20
Amsler-Krumeich Classification	
Grade 1	19 (20.2)
Grade 2	39 (41.5)
Grade3	12 (12.8)
Grade 4	24 (25.5)
BDI Classification	
Minimal	62 (66.0)
Mild	19 (20.2)
Moderate	9 (9.6)
Severe	4 (4.3)
BAI Classification	
Minimal	50 (53.2)
Mild	24 (25.5)
Moderate	10 (10.6)
Severe	10 (10.6)

UDVA: uncorrected distance visual acuity, CDVA: corrected distance visual acuity, K1:, K2:....., CCT: Central Corneal Thickness,

classification as stage I (*n* = 19, 20.2%), stage II (*n* = 39, 41.5%), stage III (*n* = 12, 12.8%), or stage IV (*n* = 24, 25.5%).

The results demonstrated that 81 (86.1%) patients had minimal-mild depression, and 13 (13.8%) patients had moderate-severe depression according to the cutoff scores of the BDI scale. The BAI scale scores revealed that 74 patients (78.7%) had minimal-mild anxiety, and 20 patients (21.2%) had moderate-severe anxiety.

According to SCID-1 interviews, a psychiatric diagnosis was present in 35 (37.2%) of 94 participants. The distribution of psychiatric diagnoses was as follows: major depression (*n* = 16, 17%), obsessive-compulsive disorder (*n* = 6, 6.4%), social phobia (*n* = 5, 5.3%), generalized anxiety disorder (*n* = 4, 4.3%), panic disorder (*n* = 2, 2.1%), specific phobia (*n* = 2, 2.1%), and dysthymia (*n* = 1, 1.1%). The most frequently occurring diagnosis was major depression.

3.1. Keratoconus severity and psychiatric diagnosis

The severity of keratoconus was measured using three different measures: the Amsler-Krumeich classification, binocular vision (<0.4 and ≥ 0.4 logMAR), and Ksteep (<52D and ≥ 52 D). The more severe the keratoconus is, the psychiatric diagnoses as determined with SCID were significantly higher (Ksteep, *p* < 0.02; CDVA, *p* < 0.04; Amsler-Krumeich, *p* < 0.007). The results are shown in Fig. 1.

3.2. Effect on QoL measures

Having a SCID-1 psychiatric diagnosis did not significantly affect the NEI-RQL-42 questionnaire scores. Binocular CDVA had no significant impact on either the overall score or any subscale scores (*p* > 0.05). KC grade and Ksteep ≥52 D in the worst eye significantly predicted lower subscale scores in far vision and near vision. Multivariate correlations between NEI-RQL-42 scores and disease indicators of keratoconus severity are presented in Table 2.

Patients with SCID-1 psychiatric diagnoses scored lower on the physical functioning, role limitations due to emotional problems, energy/fatigue, emotional well-being, social functioning, and pain subscales of the SF-36. The comparison of SF-36 scores with and without a psychiatric diagnosis according to SCID-1 in patients with keratoconus is shown in Table 3.

The overall scores on the NEI-RQL questionnaire were positively correlated with all subscales of the SF-36.

4. Discussion

Our study sample had a mean age of 23.9 ± 4.8 years, and 40 (42.6%) participants were women. Keratoconus affects both sexes. Although there are studies showing that keratoconus is more common in men, it is not yet clear whether there is a sex difference [25]. Keratoconus usually starts at puberty, and population-based studies have shown a mean age of 28.3 years at the time of keratoconus diagnosis [26]. Therefore, it should be considered that our study group was relatively young, with relatively more men than women (57.4% vs. 42.6%).

In the present study, 35 (37.2%) of 94 participants had a psychiatric diagnosis according to SCID-1. Psychiatric morbidity in chronic physical diseases has been studied extensively. The data on these comorbidities are very heterogeneous, and the prevalence rates range from 12.0% [27] to 68% [28,29]. In developed and developing countries, more than 25% of individuals have one or more mental or behavioral disorders during their lifetime. The prevalence of psychiatric disorders in the general population has been reported to be approximately 17.2% in Turkey [30]. Thus, the psychiatric morbidity of patients with keratoconus is much higher than that in the general population and is comparable to that of patients with other chronic physical diseases. The prevalence of psychiatric disorders in eye diseases is not known because no previous studies have explored this topic with a semistructured interview. The psychiatric comorbidity of medical disorders is clinically important

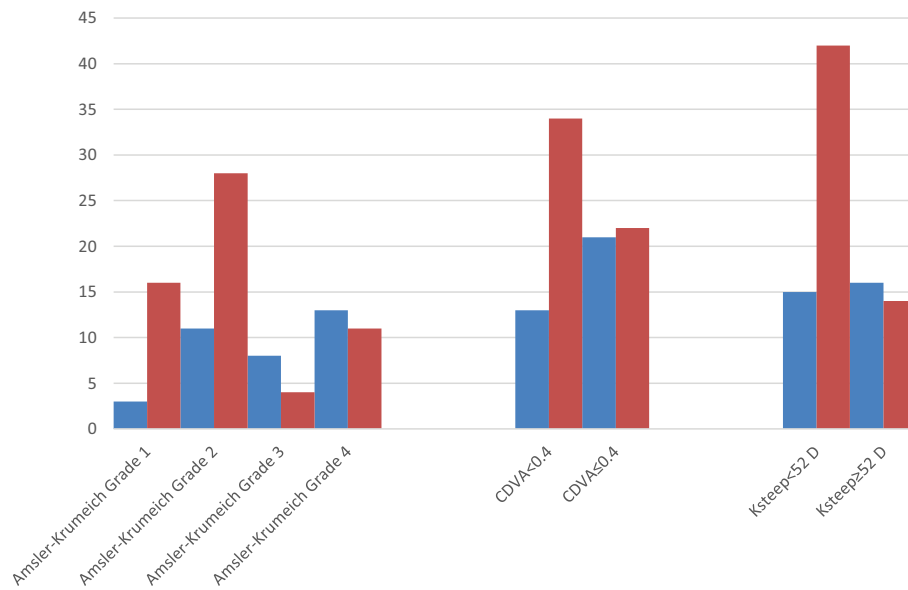


Fig. 1. Keratoconus severity and psychiatric diagnosis percentages with SCID.

Table 2

Multivariate correlations between NEI-RQL-42 scores and disease indicators of keratoconus severity.

	Binocular CDVA		Amsler-Krumeich		Ksteep	
	p value	Adjusted r2	p value	Adjusted r2	p value	Adjusted r2
Clarity of vision	0.293	0.001	0.090	0.038	0.984	-0.012
Expectations	0.722	-0.010	0.636	-0.014	0.242	0.004
Near vision	0.058	0.033	0.021	0.072	0.013	0.059
Far vision	0.074	0.025	0.006	0.098	0.009	0.067
Diurnal fluctuations	0.132	0.015	0.439	-0.003	0.935	-0.012
Activity limitations	0.056	0.034	0.138	0.028	0.360	-0.002
Glare	0.261	0.003	0.161	0.024	0.855	-0.011
Symptoms	0.734	-0.010	0.346	0.004	0.347	-0.001
Dependence on correction	0.568	-0.008	0.090	0.038	0.780	-0.011
Worry	0.207	0.007	0.814	-0.023	0.344	-0.001
Suboptimal correction	0.533	-0.007	0.598	-0.012	0.258	0.003
Appearance	0.564	-0.008	0.559	-0.010	0.934	-0.012
Satisfaction with correction	0.295	0.001	0.588	-0.012	0.731	-0.010
Overall score	0.109	0.018	0.094	0.037	0.576	-0.008

because it is generally associated with poorer medication compliance and worse outcomes [31]. It has been observed that patients with eye diseases generally do not report psychiatric or emotional problems related to eye problems to their physicians. Depression may cause poorer adherence to treatment and progression of irreversible vision loss, resulting in a more pronounced depressive status [32].

According to the BDI and BAI scales, 13 (13.8%) patients had moderate-severe depression, and 20 (21.2%) patients had moderate-severe anxiety. The studies conducted with screening scales demonstrated a psychological morbidity prevalence of 19% to 23% among different ophthalmic patients [33,34]. One study used the Zung Depression Scale and Patient Health Questionnaire-9 (PHQ-9) to assess the psychological aspects of 56 patients with keratoconus [35]. The results showed that patients had higher depression scores than the controls; 28.6% from the patient group had moderate depression and

Table 3

Comparison of SF-36 scores with and without a psychiatric diagnosis according to SCID-1 in patients with keratoconus.

SF-36 domain	Psychiatric diagnosis (+)		z	P value
	mean ± SD (n = 59)	Psychiatric diagnosis (-)		
Physical function	80.73 ± 19.69	90.59 ± 13.64	-2.835	0.005
Role limitation-physical	58.28 ± 39.92	73.30 ± 34.07	-1.928	0.054
Pain	66.02 ± 20.36	76.96 ± 19.15	-2.513	0.012
General Health	54.77 ± 21.42	62.27 ± 19.55	-1.535	0.125
Energy/vitality	45.85 ± 20.88	64.15 ± 18.75	-3.935	<0.001
Social functioning	63.18 ± 28.24	86.35 ± 19.26	-4.386	<0.001
Role limitation-emotional	49.39 ± 39.87	74.42 ± 31.84	-2.958	0.003
Mental Health	54.51 ± 22.06	70.38 ± 15.94	-3.516	<0.001

12.5% had severe depression according to the PHQ-9, whereas only 7.2% had moderate depression according to the Zung Depression Scale (ZDS). Although the depression rates measured with those scales seem to be similar to our study, it is not easy to compare our results with the other studies because different scales were used in a different age group (the mean age of patients with keratoconus was 41 ± 7 years in Moschos et al.'s study) [23]. In contrast, in a study investigating the prevalence of depression in different eye diseases with ZDS, keratoconus was not significantly associated with increased depression scores [17]. According to meta-analysis studies, the overall pooled prevalence of depression or depressive symptoms with eye disease was 25% [35]. However, all of these studies used screening tools, and most only focused on depressive symptomatology. The use of a semistructured interview tool such as SCID-1 increases the reliability of our findings. Our results also showed that the more severe the keratoconus is, the more psychiatric disorder is diagnosed. An increase in psychiatric comorbidity with the increasing severity of primary chronic physical disorders is valid for many disorders [29,36]. Studies in ophthalmologic diseases have also shown an increase in depression and anxiety symptoms with a decrease in visual function [23,37].

We also looked for the effect of having a psychiatric diagnosis on QoL measures. Interestingly, having a SCID-1 diagnosis had no significant effect on NEI-RQL-42 scores. Conversely, patients with a psychiatric diagnosis had worse QoL on the physical functioning, role limitations

due to emotional problems, energy/fatigue, emotional well-being, social functioning, and pain subscales of the SF-36. Although these two scales seem to overlap in certain areas, the SF-36 assesses general QoL, and vision is beyond the scope of this instrument. The NEI-RQL-42 was designed specifically to assess the impact of refractive error and its correction on vision-related functioning [21]. The results should be evaluated in this context because the functionalities evaluated by these two scales are different from each other.

Several studies regarding the impact of keratoconus on VRQoL using the NEI-VFQ-25 have reported that all subscale scores were significantly lower in patients with keratoconus than in controls [7,37,38]. However, Vitale (CLEK study) [39] emphasized that the NEI-VFQ was not sensitive enough to detect important QoL issues and suggested that the NEI-RQL-42 questionnaire might be more appropriate to evaluate these patients. In this study, NEI-RQL-42 scores were not found to be related to binocular visual acuity. Our findings suggested that patients with moderate and severe keratoconus had lower NEI-RQL-42 scores in near and far vision. Comparison of studies is difficult because of different patient populations, and different questionnaires were used. Panthier et al. [40] used the NEI-VFQ-25 in their study, and low distance-corrected visual acuity in the better eye was the strongest predictor of low VRQoL, which seems to be concordant with our study. A study conducted in the Turkish population [22] found that the NEI-VFQ-25 subscale scores had no significant association with keratoconus grades. However, Mahdaviyazad et al. [41] reported that patients with CDVA ≥ 0.5 logMAR in the better eye had significantly lower NEI-VFQ composite scores, and patients with severe keratoconus (steep K readings ≥ 52) had lower NEI-VFQ scores on the mental health and dependency subscales ($p < 0.05$).

4.1. Limitations

The cross-sectional design of the study is our first limitation; it was not possible to observe psychiatric morbidity in the follow-up period. Second, these findings may not be generalizable to all patients with keratoconus because our patients were mostly young, and the entire patient group was from one center. In addition, a subgroup of patients was excluded from the study due to the time criterion and refusal to participate, which might have naturally affected our results. Third, the lack of a control group is another limitation of the present study. Last, the majority of our patient sample was male. Keratoconus affects both sexes, and some studies found a higher prevalence of keratoconus in men, yet other studies reported the opposite [1,25]. This sex preponderance should be taken into account when evaluating our results.

Despite these limitations, the present study is the first to evaluate the psychiatric morbidity of patients with keratoconus using a structured psychiatric interview. Keratoconus generally affects young adults, and the magnitude of its public health impact is disproportionate to its prevalence and clinical severity, unlike other chronic ocular diseases. Over the last decades, increased attention has been given to the assessment of patient-centered outcomes, most prominently QoL in clinical studies. The present study demonstrated a high percentage of psychiatric morbidity in this patient group. Moreover, having a psychiatric disorder was associated with poorer QoL, as measured using the SF-36. These findings suggest that paying attention to psychiatric disorders in patients with keratoconus is very important. Ophthalmologists should ask patients about their mental and emotional status, which may be useful for identifying patients in need of particular psychiatric consultation and psychological support.

Declaration of Competing Interest

The authors have no affiliation with or financial interest in any organization that might pose a conflict of interest directly relevant to the contents of the paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jpsychores.2021.110384>.

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