Prevalence of Keratoconus among Young Arab Students in Israel

Einat Shneor, Michel Millodot, Ariela Gordon-Shaag, Maron Essa, Miriam Anton, Ramez Barbara, Adel Barbara

ABSTRACT

Purpose: To determine the prevalence of keratoconus (KC) in an Arab population in Israel.

Materials and methods: Videokeratography was performed on volunteer students from the Academic Arab College of Education, in Haifa, Israel. All participants filled out a self-administered questionnaire to evaluate possible risk factors for KC. Univariate and multivariate analysis were performed.

Results: Data of 314 participants were analyzed and a prevalence of (N = 10), 3.18% (95% CI, 1.2 to 5.1%) was found. The only significant factor (both in univariate and multivariate analysis) that was associated with KC was parental consanguinity (OR 5.10, p = 0.02). Druzes and Bedouins had a higher prevalence than Muslims and Christians. However, the differences were not significant possibly due to the small size of the sample.

Conclusion: The result of this study was similar to other studies conducted in the Middle East, which indicate a higher prevalence of KC than in western countries. It is also recommended that people who have consanguinity in their family should be topographically tested to detect the early stages of KC.

Keywords: Keratoconus, Consanguinity, Videokeratography.

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INTRODUCTION

Keratoconus (KC) is a corneal disorder of uncertain etiology in which the central portion of the cornea becomes thinner and bulges forward in a cone-shaped fashion resulting in myopia, irregular astigmatism and eventually visual impairment.1-3 The disease has its usual onset at puberty and in many cases progresses until the third and fourth decade of life when it usually arrests.3,5,6

In the last few years, there have been several reports of prevalence rates of KC, which have revealed large differences based on geographical locations and ethnic groups. Generally, countries with sunny and warm climates, such as India,7 Israel,8 Lebanon,9 Iran,10,11 Saudi Arabia12 and Australia13 have been found to have higher prevalence than cooler countries such as the USA, Europe and Russia.14-20 This large discrepancy could be accounted for by the different amount of sun exposure prevailing in these countries, since, ultraviolet light as a source of oxidative stress could play a role in the etiology of the disease.21 However, to the best of our knowledge there has not been a study relating an association between KC and sun exposure.

Another consideration could be the ethnic differences of the populations in these countries. Indeed in two surveys done in the UK, Asians (Bangladeshis, Indians and Pakistanis) were found to have a KC prevalence 4.4 and 7.5 times greater than white Caucasians.18,19 Likewise, Japanese have been reported to have a prevalence of KC less than one-third that of white Caucasians.22 Prevalence was 2.5% in a Persian ethnic group and 7.5% among non-Persians (Arabs, Kurds, Turks) in Iran,10 and in a comparison of the three major ethnic groups of Singapore (Chinese, Malays and Indians), Indians had significantly steeper corneas than the other groups.23 Endogamy and/or consanguinity would appear to play a major role in these communities, as was shown in a recent study.24 However, ethnic differences do not appear to prevail universally since similar KC prevalence was observed in India7 and China.25 In a study of prevalence conducted in Israel8 there was a small but not statistically significant difference between Israeli, Arabs and Jews. This lack of significance could have been due to the large difference in sample size, being n = 200 for Arabs and n = 766 for Jews. Thus, it was felt that a larger sample size of Arabs was warranted and this study aims to evaluate the true KC prevalence of an Arab population in Israel as well as to ascertain some of the risk factors of the disease.
MATERIALS AND METHODS

The student population of the Academic Arab College of Education was chosen for this survey. The college is located in Haifa, Israel and has a student body of approximately 2,500, exclusively from Arabic-speaking ethnicities.

All students received an e-mail inviting them to participate in this non-invasive screening test for KC with a short explanation of the signs and symptoms of the disease and that in the early stages there may be no visual symptoms. The e-mail stressed that it is important for all students to be tested.

Students who participated in the screening study were asked to complete an anonymous self-administered questionnaire, based on one used previously.8,24,26-28 The questionnaire included questions relating to age, sex, domicile, family history of KC, contact lens wear, sun-glasses, relation between the parents and relation of the father’s parents, allergies and eye rubbing. Ethnicity was determined by questions on religion (Christian, Muslim, Druze, else) and whether or not they define themselves as Bedouin. Muslim Arabs were classified as a different ethnicity than Muslim Bedouins.59

Exclusion criteria were subjects with contact lens wear, who had undergone refractive or corneal surgery (except for KC management), who had been diagnosed with an ocular disease other than KC and who worm hard contact lenses. Students with Arab parent were included in the study. The nature of the study was explained to the students before signing an informed consent form. The study followed the tenets of the Declaration of Helsinki and was approved by Hadassah College ethics committee. The survey was carried out between December 2012 and April 2013 and both males and females, between the ages of 18 and 60, were surveyed.

Data Collection

Videokeratography was performed on both the eyes of each subject using a TMS-4 corneal topographer (Tomey Corp. Nagoya, Japan). The test was performed by an optometry student trained in the correct use of the instrument with the supervision of a registered optometrist. Contact lens wearers were asked to remove them immediately prior to the examination. Proper fixation and alignment were ascertained when the cross-hair was in the center of the pupil. Two images of each eye were taken and the best topographic image that displayed the largest area of cornea and had the least distortions was selected.

The Tomey TMS-4 Topographic Modeling System includes KC screening software which provides KCI and KPI indices. These indices have been shown to have high sensitivity and specificity.30 The color-coded corneal map of each participant was examined by three investigators who were blind to the results of the questionnaire. The dioptic power of the corneal apex and the maximum dioptric difference between the corneal apex and a spot in the middle of the superior half of the cornea (IS) was calculated as well. On the basis of the videokeratographic indices and the clinical assessments an eye was defined as manifest KC if it fulfilled the following: KSI > 0%; KPI > 0%; clear topographic pattern; corneal apex > 50D and/or IS > 3.5D.8

STATISTICAL ANALYSIS

Prevalence and 95% confidence intervals (CI) of all subjects, males and females were calculated. If a person had KC in one eye only or both eyes, that person was defined as having the disease. Univariate analyses were performed using standard non-parametric and parametric tests (Fisher’s exact test if any of the expected frequencies was less than 5, and the t-test) to determine whether sex, ethnicity, family history of KC, sunglasses, education, parent’s relatives, atopy or eye rubbing were significantly associated with KC. Multivariate logistic regression analysis was performed to explore the association between KC (the outcome variable) and the independent predictors, which had been found significant in the univariate analysis using a statistical software package. The predictor variables were binary and coded as ‘1’ (KC present) and ‘0’ (KC absent), ‘1’ for male and ‘0’ for female. Adjusted odds ratios (OR) as a measure of association while controlling for the effects of the other predictors, and 95% confidence intervals (CI) were calculated. All tests were two-tailed and p values lower than 0.05 were considered statistically significant.

RESULTS

A total of 450 students (18% of the total number of students in the college) volunteered to participate in the study. Despite the fact that the examiners encouraged the subjects to participate in all aspects of the study, there was not 100% compliance and 136 subjects were excluded, because, they did not fill out the questionnaire and/or had very poor photographic images and/or did not undergo imaging. As a result, a total of 314 met the eligibility criteria, were examined and completed the questionnaire. The mean (SD) age of the participants was 25.05 ± 8.83 (range 18-60) with 38 (12.1%) males and 276 (87.9%) females and the former were significantly older than the latter (31.19 ± 13.41 for males vs 24.23 ± 7.68 for females; p < 0.001). Out of the participants, 35 (11.15%) were Christian, 179 (57.01%) were Muslim, 65 (20.70%) were Druze and 33 (10.51%) were of Bedouin origin (Table 1).

Table 2 gives the characteristics of the KC and control groups. KC was found in 10 subjects (16 eyes, 9 right eyes, 7 left eyes) individuals representing a prevalence of 3.18% (95% CI, 1.2-5.1%). Six subjects had KC in both eyes. KC
The prevalence of Keratoconus among Young Arab Students in Israel

Prevalence was found to be 2.90% (95% CI, 0.9-4.9%) in women and 5.26% (1.8-12.3%) in men, but this was not statistically significant (p = 0.35, Fisher’s test). Six (60%) subjects out of the 10 subjects diagnosed with KC did not know about their condition.

The steepening was located inferiorly in all eyes. All keratoconic eyes had irregular astigmatism. In all 10 cases the KCI and KSI indices were indicative of KC. The mean (SD) corneal power of the apex of the cone of the most severely affected eye of each subject was 50.02 ± 4.10D and the I-S was 8.64 ± 3.52D.

The prevalence of KC in Muslims (excluding Bedouins) was 2.2% (CI 0.05-4.3%), in Druzes 4.6% (CI 0.5-9.7%), in Christians 2.9% (CI 0.1%-5.7%) and in Bedouins 6.1% (CI 2.04-14.2%). The results are summarized in Table 2.

Table 1: Ethnic groups, gender and age of sample population

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Muslim</th>
<th>Druze</th>
<th>Christian</th>
<th>Bedouin</th>
<th>Other</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (%)</td>
<td>179 (57)</td>
<td>65 (20.7)</td>
<td>35 (11.2)</td>
<td>33 (10.5)</td>
<td>2 (0.6)</td>
<td>314</td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>23.8 (7.3)</td>
<td>24.5 (7.4)</td>
<td>33.8 (13.9)</td>
<td>21.6 (2.1)</td>
<td>24 (0)</td>
<td>25.05 (8.83)</td>
</tr>
<tr>
<td>Female</td>
<td>163</td>
<td>55</td>
<td>30</td>
<td>26</td>
<td>2</td>
<td>276</td>
</tr>
<tr>
<td>Male</td>
<td>17</td>
<td>10</td>
<td>5</td>
<td>6</td>
<td>0</td>
<td>38</td>
</tr>
</tbody>
</table>

Table 2: Prevalence of KC in the different groups

<table>
<thead>
<tr>
<th>Group</th>
<th>KC (%)</th>
<th>Normal</th>
<th>All</th>
<th>Prevalence KC (%)</th>
<th>95% CI</th>
<th>95% CI</th>
<th>OR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects</td>
<td>10</td>
<td>304</td>
<td>314</td>
<td>3.18</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range—Age (years)</td>
<td>19-28</td>
<td>18-60</td>
<td>18-60</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average age (SD)</td>
<td>25.1 (8.8)</td>
<td>25.2 (8.9)</td>
<td>25.1 (8.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male—N (%)</td>
<td>2 (20)</td>
<td>36 (11.8)</td>
<td>38 (12.2)</td>
<td>5.26</td>
<td>0.38</td>
<td>9.11</td>
<td>1.86</td>
<td>0.346 * (Male vs Female)</td>
</tr>
<tr>
<td>Male—Average age (SD)</td>
<td>23.50 (15.9)</td>
<td>31.63 (13.4)</td>
<td>31.19 (13.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female—N (%)</td>
<td>8 (80)</td>
<td>268 (88.2)</td>
<td>276 (87.9)</td>
<td>2.90</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female—Average age (SD)</td>
<td>21.57 (10)</td>
<td>24.30 (7.6)</td>
<td>24.24 (7.7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muslim† (%)</td>
<td>4 (40)</td>
<td>175 (57.6)</td>
<td>179 (57)</td>
<td>2.2</td>
<td>0.14</td>
<td>1.78</td>
<td>0.49</td>
<td>0.337 * (KC vs Control)</td>
</tr>
<tr>
<td>Druze (%)</td>
<td>3 (30)</td>
<td>62 (20.4)</td>
<td>65 (20.7)</td>
<td>4.6</td>
<td>0.42</td>
<td>6.66</td>
<td>1.67</td>
<td>0.437 *</td>
</tr>
<tr>
<td>Christian (%)</td>
<td>1 (10)</td>
<td>34 (11.2)</td>
<td>35 (11.1)</td>
<td>2.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bedouin (%)</td>
<td>2 (20)</td>
<td>31 (10.2)</td>
<td>33 (10.5)</td>
<td>6.1</td>
<td>0.45</td>
<td>10.30</td>
<td>2.2</td>
<td>0.283 *</td>
</tr>
<tr>
<td>Other (%)</td>
<td>0 (0)</td>
<td>2 (0.7)</td>
<td>2 (0.6)</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Fisher’s test; ** t-test; † excluding Bedouin

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Table 3 presents the univariate results of the various independent factors evaluated in KC and controls. Neither eye rubbing, allergy, sex, religion, family history of KC and habitual wear of sunglasses were found not to be significant.

A significant association was only found between KC and parental first-cousin consanguinity (Fisher’s test, p = 0.017, OR 5.08, CI 1.42-18.20), between KC and father’s parental first-relation consanguinity (Fisher’s test, p = 0.006, OR 4.00, CI 1.94-25.31,) and for more than 16 years of education (Fisher’s test, p = 0.011, OR 9.59, CI 2.22-41.40). The multivariate logistic regression was performed with only 2 variables: parental first-cousin consanguinity and education for more than 16 years of education, because of the intra-dependence between parents and first-relation consanguinity. We found only parental first-cousin consanguinity to be significant (OR 5.10, 95% CI 1.41-18.33, p = 0.02).

**DISCUSSION**

This study assessed the prevalence of KC in a population of Arab students in Haifa, Israel. A prevalence of 3.18% (95% CI) was found, with a higher, but not statistically significant prevalence for men. These results are consistent to the results of other recent population studies in Israel, Iran, Lebanon and Saudi Arabia (Table 4). This is in contrast to studies from Western countries that demonstrate a lower prevalence.

The current study identified consanguinity as a significant risk factor for KC in Israeli Arabs. Gordon-Shaag et al found similar results for Palestinian Arabs. While the studies in Iran, Lebanon and Saudi Arabia did not address this issue, these countries are known for a high degree of consanguinity. Taken together, this indicates a genetic autosomal recessive pathogenesis for the disease, at least in this region. The genetic etiology is supported by three additional lines of evidence. First, KC patients report a positive family history of the disease although it was not evident in our study possibly because of the small sample. Second, is the report of KC concordance between monozygotic twins.

Third, is genetic linkage analysis and association studies.20,41,50-65
This study identified an association between KC and years of education, similar to a previous study in the region. The reason is still not clear, but may be an ascertainment bias as more educated people are more likely to participate in such a research study.

There are several limitations to this study. The sample size may be too small to provide a precise estimate of the prevalence of KC. In addition, the small sample size resulted in only ten subjects with KC, which lowers the power when identifying risk factors. The data tended to indicate the higher prevalence in Druzes and Bedouins, but this result needs to be viewed with caution because of the very small sample. It must be noted though, that these ethnic groups live in small villages were consanguinity and endogamy are common, a known risk factor for KC. Further research is needed to corroborate the results of this study. The sample population is a non-random group of individuals obtained from college students in Haifa who voluntarily presented themselves for a corneal topographic examination and questionnaire. A selection bias may have occurred since individuals who knew they had the disease may have refrained from participating in the study because they were under ophthalmic care, while others with visual problems may have been more likely to volunteer. As in most studies, the assessment of risk factors depended on the information given in the self-administered questionnaire, which may be biased by the fact that the ability of subjects to report earlier experiences differs.

### CONCLUSION

We recommend that children who have consanguinity in the family should do topography of the cornea at a young age in order to detect early stages of KC, especially as in this study 60% of the detected cases were unaware that they had the disease.

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REFERENCES