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## Prevalence and associated factors of pinguecula in western Turkey

### *Batı Türkiye'de pinguekula prevalansı ve ilişkili faktörler*

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#### Abstract

**Purpose:** This study aimed to describe the prevalence and factors associated with pinguecula in the western part of Turkey.

**Materials and methods:** The study included 1443 participants over the age of 20 between January 2018 and October 2019. The presence of pinguecula on slit lamp examination was recorded. A structured questionnaire which includes basic demographic data, occupational activity, educational level, alcohol consumption and smoking, dry eye questionnaire and systemic disorders such as diabetes or hypertension was applied.

**Results:** The prevalence of pinguecula was 52.5%. Pinguecula prevalence was higher in males (58.4%) than females (46.8%). The prevalence of pinguecula significantly increased with age ( $p<0.001$ ). Outdoor working, more than 2 hours of sun exposure and decreased tear break-up time (TBUT) values increase the prevalence rate of pinguecula. The pinguecula prevalence decreases as the level of education increases.

**Conclusion:** The prevalence of pinguecula was detected in 52.5% of the population aged  $\geq 20$  years and this is the first study which investigates the prevalence of pinguecula in Turkey. Age, gender, duration of sun exposure, TBUT values and education level are found to be related to the pinguecula prevalence. We also found that pinguecula causes lower TBUT scores due to instability of tear film despite normal tear film secretion and volume.

**Key words:** Pinguecula, prevalence, Turkey.

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#### Özet

**Amaç:** Bu çalışmada Türkiye'nin batı bölgesindeki pinguekula prevalansı ve ilişkili risk faktörlerinin araştırılması amaçlandı.

**Gereç ve yöntem:** Çalışmaya Ocak 2018 ile Ekim 2019 tarihleri arasında 20 yaş üstü 1443 katılımcı dahil edildi. Biomikroskopik muayene ile pinguekula varlığı ve lokalizasyonu kaydedildi. Temel demografik verileri, mesleki aktivite, eğitim düzeyi, alkol tüketimi ve sigara kullanımı, kuru göz anketi ve diyabet veya hipertansiyon gibi sistemik bozuklukları sorgulayan bir anket uygulandı.

**Bulgular:** Pinguekula prevalansı %52,5 olarak tespit edildi. Pinguekula prevalansı erkeklerde (%58,4) kadınlardan (%46,8) daha yüksekti. Pinguekula prevalansında yaşla birlikte anlamlı derecede artış saptandı ( $p<0,001$ ). Dış mekânda çalışma, 2 saatten fazla güneşe maruz kalma ve azalmış gözyaşı parçalanma süresi (TBUT) değerleri ile pinguekula prevalansının arttığı tespit edildi. Pinguekula prevalansının eğitim seviyesi arttıkça azaldığı belirlendi.

**Sonuç:** Bu çalışma Türkiye'de pinguekula prevalansını araştıran ilk çalışma olup 20 yaş üzeri popülasyonda pinguekula prevalansını %52,5 olarak tespit ettik. Yaş, cinsiyet, güneşe maruz kalma süresi, TBUT değerleri ve eğitim düzeyi pinguekula prevalansı ile ilişkili bulunmuştur. Ayrıca pinguekula hastalarda normal gözyaşı salgılanması ve hacmine rağmen gözyaşı film bozukluğuna yol açtığını tespit ettik.

**Anahtar kelimeler:** Pinguekula, prevalans, Türkiye.

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## Introduction

Pinguecula is a fibrous, yellowish, slightly elevated, fleshy degenerative thickening of the bulbar conjunctiva close to the cornea. Pinguecula develops as a result of an alteration of connective tissue, where stromal collagen is replaced with thicker fibers [1-5]. Albeit pinguecula resembles lipid deposition, histopathological studies show that it consists of basophilic, degenerate, subepithelial tissue similar to pterygium [6].

Pinguecula is usually asymptomatic, but sometimes causes ocular irritation, foreign body sensation and often a cosmetic effect that is the main concern of patients. Pinguecula can be frustrating because there is no effective medical or surgical treatment. Albeit there is limited report on the prevalence of pinguecula, current results show a high prevalence; in some regions it is reported to be as high as 70% [7, 8].

The etiology and pathogenesis of this common degenerative disease in the conjunctiva is still unclear. There are many risk factors for the development of pinguecula including age, UV radiation [9-12], high cholesterol metabolism [13], exposure to dust [14], elastotic degeneration [15], alcohol intake [9] and dry eye [3]. To our knowledge, this is the first study which investigates the prevalence of pinguecula in Turkey. Hereby, we present the prevalence of pinguecula, and its relationship with systemic and ocular diseases and lifestyle factors.

## Materials and methods

This study was approved by the ethics committee of Faculty of Medicine, Dokuz Eylül University (protocol number/date; 2018/16-31/28.06.2018) and conformed to the Declaration of Helsinki and received participants' approval. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research. Written informed consent was obtained from all the eligible subjects.

This study was performed in Izmir that is located in 38 degrees north of the equator. Izmir, a province in the western part of the Republic of Turkey, is bordering the Aegean Sea. Between January 2018 and October 2019, 1443 patients over 20 years of age who agreed to participate in the study were included.

A structured questionnaire which includes basic demographic data, occupational activity, educational level, alcohol consumption and smoking, dry eye questionnaire and systemic disorders such as diabetes or hypertension was administered. All subjects were successively evaluated by an ophthalmologist (HD). The diagnosis of pinguecula was made when the typical yellowish lesion that forms on the nasal or temporal conjunctiva was present. Particular attention was paid to pterygium, pseudopterygium and conjunctival neoplasm, which can be confused with pinguecula.

Occupational activity was evaluated on the basis of average daytime sun exposure experienced. Participants were grouped as predominantly outdoor workers or indoor workers. Occupations where most of the day are spent in outdoor light are classified as outdoor work. Indoor workers were those who spent most of the day indoors such as office, hospital. Participants were also divided into two groups according to whether the exposure to daily sunlight was more than 2 hours [16]. The level of education was categorized into the stages of illiterate, primary school education, high school education and university.

The ocular examinations were performed at the same location by the same ophthalmologist (HD) using the same instruments. A comprehensive anterior segment examination was performed under a slit lamp microscope. The diagnosis of pinguecula was made when the typical lesion was present. For tear breakup time (TBUT), Standard 1 mg sodium Paper strips containing fluorescein (Fluorets, Smith Nephew) were used. The patient was asked to open and close his eyes several times, allowing the fluorescein to spread smoothly into the tear film layer. The time interval between the last blink and the appearance of the first corneal dark spot was determined. This measurement is repeated three times and the average value was recorded. For Schirmer I test, tear flow was measured with filter paper Schirmer test strip for 5-minutes without anesthetic in both eyes.

## Statistical analysis

For calculating the 95% confidence intervals (CI), the cluster sampling design effect was considered. We used the multiple logistic

regression test to examine the association of pinguecula with age, gender and smoking. The Chi-square test was used to study the association between pinguecula and work place (indoor vs. outdoor) and education level. SPSS version 22.0 for windows (SPSS Inc, Chicago, IL, USA) was used. The level of significance was set at  $p < 0.05$  for all analyses.

## Results

In this study, 726 (50.3%) of 1443 participants were female. The prevalence of pinguecula was 52.5% (95% CI 49.5-55.5%). There were 759 persons with either unilateral (n:103, 13.5%) or bilateral (n:656, 86.5%) pinguecula. Pinguecula more frequently located to nasal conjunctiva (83.7%). In 26.7% of the eyes, pinguecula located on both nasal and temporal conjunctiva.

Pinguecula prevalence increased significantly with age ( $p < 0.001$ ) and was higher in males (58.4%) than females (46.8%) (OR 1.59, 95% CI 1.29-1.96) (Table 1). Comparisons between age subgroups are presented in Table 2, indicating that the highest prevalence was found in participants aged 60-69 years.

About half of the participants (791/1443, 54.8%) were either illiterate or only completed primary school. Higher educational level was a protective factor for pinguecula (OR 0.57, 95% CI 0.38-0.91). 28.2% of our patients were office workers and 48.6% of our patients were involved in jobs in which they were exposed to sunlight more than 2 hours a day (Table 1). Pinguecula prevalence was less in indoor workers such as office workers in comparison to outdoor workers (OR 0.20, 95% CI 0.13-0.29). Among all the patients, the ones that exposure direct sunlight more than two hours daily (727/1443, 50.3%) are most likely to have pinguecula (OR 4.03, 95% CI 3.22-5.05). Table 1 shows the detailed demographic characteristics of our cases.

OSDI score was higher in participants with pinguecula ( $18.87 \pm 17.0$ ) than participants without pinguecula ( $8.8 \pm 10.6$ ) ( $p < 0.000$ ) but no association was found ST 1 ( $p = 0.996$ ). Pinguecula prevalence was higher in patients with low TBUT measurements ( $p = 0.001$ ) (Table 1).

There was no association between alcohol consumption, smoking, diabetes mellitus, hypertension and pinguecula prevalence (Table 1).

## Discussion

To the best of our knowledge, this is the first study which is investigating the prevalence of pinguecula in Turkey. We conducted this study in Izmir (Western part of Turkey) that is located in 38 degrees north of the equator. In this study, pinguecula was detected in 52.5% of the population aged  $\geq 20$  years. Studies on this subject are rare and many are summarized in Table 3. According to the previous studies, the prevalence of pinguecula varies highly around the world, ranging from 6.2-90% [9-12, 16-19]. Possible reasons for this variable results might be due to different age ranges of the studies, different ethnic backgrounds, different smoking and alcohol use habits, and different environmental factors such as latitude of the study regions.

Age has been shown to have strong correlation with pinguecula formation by many studies [9-12, 16-19] (Table 3). On the contrary to these studies, Asokon et al. [11] reported that increasing age was not associated with the prevalence of pinguecula. Their study participants were over 40 years of age and the prevalence of pinguecula was higher in the 50-59 age group. They suggested that a pinguecula can develop into a pterygium and this could be the reason for the decreased prevalence of pinguecula with age. In the current study, our participants were over 20 years of age, and the prevalence of pinguecula increased with age until 6<sup>th</sup> decade. There was a significant decrease in pinguecula prevalence after 7<sup>th</sup> decade supporting the hypothesis of Asokon et al. [11] Additionally, E Viso et al. [9] reported that the prevalence of pinguecula stabilized after the age of 60 years in women and after the age of 70 years in men in contrast to the prevalence of pterygium that was highest in persons aged  $> 80$  years. In agreement with previous studies, we thought that the reason for decreased pinguecula prevalence after 6<sup>th</sup> decade is due to possible progression of pinguecula to pterygium.

**Table 1.** Demographic and clinical profile of the patients

	Pinguecula n (%)	Non-pinguecula n (%)	OR (%95 CI)	p value
Gender				<b>0.001</b>
Female	340 (46.8)	386 (53.2)	Ref	
Male	419 (58.4)	298 (41.6)	1.59 (1.29-1.96)	
Working outdoors				0.001
Daily sunlight exposure <2 hours	310 (43.3)	406 (56.7)	Ref	
Daily sunlight exposure >2 hours	549 (75.5)	178 (24.5)	4.03 (3.22-5.05)	
Smoking habits				0.993
Non-smokers	250 (52.9)	222 (47.1)	Ref	
Ex-smokers	223 (52.6)	201 (47.4)	0.98 (0.75-1.28)	
Smokers	286 (52.7)	256 (47.3)	0.99 (0.77-1.27)	
Alcohol intake				0.982
Abstains	589 (53.5)	528 (46.5)	Ref	
1-14 units/week	159 (52.1)	146 (47.9)	0.97 (0.75-1.25)	
>14 units/ week	11 (52.4)	10 (47.6)	0.98 (0.41-2.34)	
Diabetes				0.560
No	658 (52.3)	600 (47.7)	Ref	
Yes	101 (54.6)	84 (45.4)	1.09 (0.80-1.49)	
Hypertension				0.299
No	559 (51.8)	520 (48.2)	Ref	
Yes	200 (54.9)	164 (45.1)	1.13 (0.89-1.44)	
Schirmer test 1				0.996
Schirmer <5 mm	118 (52.6)	106 (47.4)	Ref	
Schirmer 5-10 mm	301 (52.7)	270(47.3)	1.00 (0.73-1.36)	
Schirmer > 10 mm	340 (52.4)	308 (47.6)	0.99 (0.73-1.34)	
TBUT				0.001
TBUT >10 seconds	299 (46.4)	345 (53.6)	Ref	
TBUT 5-10 seconds	355 (54.6)	295 (45.4)	1.38 (1.11-1.72)	
TBUT<5 seconds	105 (70.4)	44 (29.6)	2.75 (1.87-4.04)	

Abbreviations: n; number of patients; CI, confidence interval; OR, odds ratio; TBUT, tear film break-up time test \*Chi square test

**Table 2.** Pinguecula prevalence by age

	Pinguecula n (%)	Non-pinguecula n (%)	OR (%95 CI)
All patient	759 (52.5)	684 (47.5)	
20-29 years	57(27.5)	150 (72.5)	Ref
30-39 years	84 (40.0)	126 (60.0)	1.75 (1.16-2.64)
40-49 years	118 (51.8)	110 (42.2)	2.82 (1.89-4.21)
50-59 years	139 (57.9)	101 (42.1)	3.62 (2.43-5.39)
60-69 years	162 (64.8)	88(35.2)	4.84 (3.24-7.23)
70-79 years	129 (63.2)	75(36.8)	4.52 (2.98-6.86)
≥80 years	70 (51.0)	67 (49.0)	2.74 (1.74-4.32)
P value	p<0.001		

Abbreviations: n, number of patients; CI, confidence interval; OR, odds ratio; \*Chi square

**Table 3.** Prevalence of pinguecula and associated factors according to countries

Study	Country	Sample (n)	Age	Pinguecula (%)	Age	Male Sex	Associated Sunlight UV	Factors Level of education	Smoking	Alcohol
Viso et al. <sup>9</sup>	Spain	619	≥40	47.9%	S	S	S	S	NS	S
Rezvan et al. <sup>10</sup>	Iran	5190	40-64	61.0%	S	S	S	S	S	NS
Asakon et al. <sup>11</sup>	India	3924	≥40	16.2%	NS	NS	S	NS	S	NS
Fotouhi et al. <sup>12</sup>	Iran	4565	≥1	22.5%	S	S	NS	NS	NS	NS
Le Q et al. <sup>16</sup>	China	959	≥50	75.5%	S	S	S	S	NS	NS
Norn <sup>17</sup>	Jordan	127	≥10	90.0%	S	NS	S	NM	NM	NM
This study	Turkey	1443	≥20	52.5%	S	S	S	S	NS	NS

S, significant; NS, not significant; NM, not mentioned



Rural residence has been shown to be strongly associated with the development of pinguecula [11, 16], since residents living in rural areas mainly undertake outdoor occupational activities, meaning far more sunlight exposure. UV radiation cause ocular surface irregularities by increasing the level of p53, proinflammatory cytokines and matrix metalloproteinase [17]. And a dose-response relationship between UV radiation and pinguecula has been demonstrated [9, 16]. We found that the prevalence of pinguecula was higher in participants who spend more than 2 hours outside per day. Participants who have outer occupational activity were also found to have a higher prevalence. These results are supporting the previous studies which supported the association between UV exposure and pinguecula formation [9-11, 16-20].

In this study, the prevalence of pinguecula according to gender was higher in men similar to previous studies [7-12]. We think this is a result of UV exposure difference between the genders in our study.

There are controversial results regarding to education level effects on pinguecula development. In some studies, it was found that the level of education was not associated with pinguecula development. In our study we found that a higher level of education is a protective factor for the development of pinguecula. The reason for this result might be that people with higher education tend to work indoors and are less exposed to UV light, thus less affected by pinguecula.

In some studies, it has been found that alcohol use and smoking have a significant effect on the prevalence of pinguecula [9, 10]. They suggested the increased oxidative stress related to alcohol intake and smoking might favor the degenerative changes associated with pinguecula formation. Nevertheless, Le Q et al. [16] reported that alcohol intake and smoking were not associated with pinguecula formation in accordance with our study.

The relationship between blepharitis, pseudoexfoliation, and meibomian gland dysfunction that makes ocular surface pathologies and disrupts the tear film functions and systematic diseases such as diabetes mellitus and high blood pressure levels were

researched and studied on many articles but there is no evidence found to increase the prevalence of the pinguecula. We also studied the relationship between hypertension and diabetes mellitus on our investigation and we found no correspondence, neither.

In previous studies, it has been suggested that surface elevation and irregularity due to pinguecula cause tear film instability and a shorter TBUT score [3, 5, 16, 21, 22]. Schirmer test results are more controversial. Although there are more studies showing that schirmer test results do not differ in patients with pinguecula [3, 5, 21, 23], there are also studies showing a significant decrease in schirmer test results [22]. However, authors attributed this decreased ST results to the possible inflammation in the eyes with pinguecula [22]. Reduced blink reflex, irregular ocular surface formation and decreased mucus secretion may cause shorter TBUT. Also squamous metaplasia on the surface of the pinguecula may disrupt the stability of the tear film. Squamous metaplasia is common in dry eye disease. It is not clear whether pinguecula disrupts tear film stability and cause dry eye disease or dry eye disease induce formation of pinguecula.

ST results are an indicator of tear film secretion and volume. In our study, schirmer test results did not differ in patients with pinguecula. In previous studies, it has been reported that pinguecula causes ocular surface irregularity and this irregularity disrupts the tear film stability despite normal tear film secretion and volume. Similar to previous studies, we found that pinguecula causes lower TBUT scores due to instability of tear film despite normal tear film secretion and volume [5, 23]. In agreement with previous studies, we found that the prevalence of pinguecula was higher in participants with lower TBUT scores. In our study, schirmer test results did not differ in patients with pinguecula.

Pinguecula may cause itching, burning and foreign body sensation similar to dry eye disease [22]. Ocular Surface Disease Index (OSDI) is a subjective survey which evaluates participants in terms of dry eye disease symptoms [16, 21]. We found that OSDI scores are higher in patients with pinguecula similar to previous. Since this is a cross-sectional study, it is not possible to make a deduction regarding to the relationship with tear film functions and

pinguecula. Longitudinal studies are needed to understand if tear film abnormalities are the precursor or the result of pinguecula.

An important limitation of this study is that we did not ask our participants if they had moved to Aegean region from another region. Izmir is a coastal city. Some of our participants might have migrated from other parts of Turkey which have different characteristics such as being a rural or mountainous area. Therefore, it is not possible to make a comment on whether these features have an impact on pinguecula prevalence. Another limitation of the study is that it is a hospital-based study that may prevent us from obtaining a representative sample of the population.

In conclusion, the prevalence of pinguecula was determined to be 52.5% in Izmir, an urban coastal area located in the western part of Turkey. The prevalence of pinguecula increases with age. Male gender and long term exposure to sun were found to be risk factors for pinguecula formation. We also found that pinguecula causes lower TBUT scores due to instability of tear film despite normal tear film secretion and volume. The effects of smoking habits, alcohol intake and dry eye disease on pinguecula formation needs further studies.

**Conflict of interest:** No conflict of interest was declared by the authors.

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**Ethics committee approval:** This study was approved by the ethics committee of Faculty of Medicine, Dokuz Eylul University (protocol number/date; 2018/16-31/28.06.2018)

#### **Authorship contributions**

Concept: H.D, C.K, Design: H.D, C.K, Data Collection or Processing: H.D, Analysis or Interpretation: H.D, C.K, Literature Search: H.D, C.K, Writing manuscript: H.D.