

## Risk Factors for Pterygium in Ilam Province, Iran

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## Abstract

**Purpose:** To evaluate the risk factors for pterygium in the dry, high altitude province of Ilam, Iran.

**Methods:** The study included patients who presented to ophthalmology clinic. The patients were divided into two groups: 210 diagnosed with pterygium or pinguecula (unilateral or bilateral), and 210 healthy controls. Demographic variables, living environment, disease type, disease laterality, family history of pterygium as well as history of smoking, working outdoors, baking, welding, ocular conditions (trachoma keratopathy, glaucoma, refractive error, and dry eye), use of glasses, ultraviolet light exposure, and systemic conditions were collected from both groups and compared for risk assessment.

**Results:** Univariate analysis revealed that age ( $P = 0.001$ ), sex ( $P = 0.001$ ), family history of pterygium ( $P = 0.001$ ), positive history of smoking ( $P < 0.001$ ), history of baking ( $P = 0.045$ ), welding experience ( $P < 0.001$ ), severe blepharitis ( $P < 0.001$ ), hyperopia ( $P < 0.001$ ), dry eye ( $P < 0.001$ ), hypertension ( $P < 0.001$ ), ischemic heart disease ( $P < 0.001$ ), obesity ( $P = 0.038$ ), and primary residential area ( $P = 0.025$ ) had significant associations with increased incidence of pterygium. However, in multivariate analysis, only family history of pterygium, cigarette smoking, history of baking, age, and severe blepharitis were significantly associated with the incidence of pterygium ( $P < 0.001$ ,  $P < 0.001$ ,  $P = 0.002$ ,  $P = 0.023$  and  $P = 0.002$ , respectively).

**Conclusion:** This study tested more risk factors related to the prevalence of pterygium compared to previous studies. It also confirmed previously established risk factors. Family history of pterygium and blepharitis were risk factors that have not been reported in previous studies and were found to be significantly associated with the development of pterygium in this study.

**Keywords:** Prevalence; Pterygium; Risk Factors

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## INTRODUCTION

Pterygium is an abnormal inflammatory fibrovascular growth extending from the interpalpebral conjunctiva to the cornea. It is a common ophthalmic disorder of unknown etiology and pathogenesis.<sup>[1-4]</sup> Pinguecula also has the same histopathological characteristics as pterygium but without corneal involvement.<sup>[5,6]</sup> Further growth of pterygium onto the cornea can cause visual impairment secondary to induced astigmatism,

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visual axis obstruction, and loss of corneal transparency.<sup>[6]</sup> Although the pathogenesis of pterygium is yet to be understood, many studies have reported its prevalence to range from 0.3% to 37.1% in different populations.<sup>[6-10]</sup> The reported prevalence of pinguecula ranges from 41% to 90%.<sup>[11,12]</sup> Reported risk factors of pterygium include: age,<sup>[11-16]</sup> sex,<sup>[11,12,14,15]</sup> exposure to ultraviolet light such as in outdoor work and lower altitudes,<sup>[17-20]</sup> and socioeconomic status, and level of education.<sup>[21,22]</sup> Environmental factors such as dust and dry weather have also been implicated as risk factors for pterygium.<sup>[23]</sup> Despite the high altitude of Ilam province, there is no available data regarding the prevalence and risk factors for pterygia in this region. The aim of this study was to identify the risk factors associated with pterygium in Ilam province in Iran.

## METHODS

The study included patients who presented to the ophthalmology clinic. Patients were divided into two groups: 210 patients with pterygium or pinguecula as the case group, and 210 healthy subjects as the controls. A comprehensive questionnaire was compiled based on relevant risk factors, demographic variables, living environment, disease type, disease laterality, familial history as well as history of smoking, drug abuse, working outdoors, baking, welding, ocular conditions (trachoma keratopathy, glaucoma, refractive error, dry eye), use of glasses, ultraviolet light exposure, residential area (urban or rural), and systemic conditions. All patients underwent ophthalmological examinations, and the questionnaires were completed by one ophthalmologist. Examinations included a thorough systemic examination and a comprehensive ophthalmic examination and refraction. Severity of dry eye was evaluated by available tests and classic grading systems such as fluorescein staining pattern and tear breakup time (TBUT) tests.

At least 394 samples were needed to have a power of 80% to detect a difference as large as 10% in the prevalence of exposure between the case and control groups when the possibility for type I error was 0.05.

To check for the normality of distribution of the data, we used the Kolmogorov-Smirnov test and quantile-quantile (q-q) plot. We presented the data as mean, standard deviation, median, range, frequency, and percentage. To evaluate the differences between groups, we used the Chi-square test, Fisher's exact test, *t*-test, and Mann-Whitney test. To evaluate the simultaneous effect of all variables and to obtain the adjusted odds ratio (AOR), we used multiple logistic regression. Then, we used the backward step selection method (based on likelihood ratio test) with entry criteria of 0.05 and exclusion criteria of 0.10. All statistical analyses were

performed using SPSS (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY:IBM Corp.).

## RESULTS

A total of 420 patients were enrolled in this study: 210 patients with pterygium/pinguecula (case group) and 210 healthy participants (control group). The mean ages of the case and control groups were  $50.8 \pm 14.8$  years (range, 20 to 92 years) and  $41.9 \pm 20.4$  years (range, 6 to 84 years), respectively. In univariate analysis, age ( $P = 0.001$ ), sex ( $P = 0.001$ ), working outdoors ( $P = 0.001$ ), family history of pterygium ( $P = 0.001$ ), positive history of smoking ( $P < 0.001$ ), history of baking ( $P = 0.045$ ), welding experience ( $P < 0.001$ ), severe blepharitis ( $P < 0.001$ ), hyperopia ( $P < 0.001$ ), dry eye ( $P < 0.001$ ), hypertension ( $P < 0.001$ ), ischemic heart disease ( $P < 0.001$ ), obesity ( $P = 0.038$ ), and primary residential area ( $P = 0.025$ ) were found to have significant associations with increased incidence of pterygium [Table 1].

The levels of education of the patients were classified into three groups: illiterate, undergraduate diploma, and diploma or higher. There was no significant association between the level of education and prevalence of pterygium ( $P = 0.791$ ).

In multivariate analysis, only family history, cigarette smoking, history of baking, age, and severe blepharitis, were significantly associated with higher incidence of pterygium ( $P < 0.001$ ,  $P < 0.001$ ,  $P = 0.002$ ,  $P = 0.023$ , and  $P = 0.002$ , respectively).

Factors such as sex ( $P = 0.537$ ), residential area ( $P = 3.00$ ), level of education [illiterate ( $P = 0.103$ ), undergraduate diploma ( $P = 0.267$ ), diploma ( $P = 0.422$ )] and ischemic heart disease ( $P = 0.242$ ) were not significantly associated with increased incidence of pterygium [Table 2].

## DISCUSSION

Despite the undetermined pathogenesis of pterygium, its risk factors are well known and have been studied extensively. Considering the geography and demographics of Ilam, the estimated prevalence of pterygium in the local population is projected to be high. Even though there have been many studies on pterygium worldwide, few have been conducted in Iran, and none have been conducted on the dry, high altitude, and inbred population of Ilam.<sup>[1-4]</sup>

In this study, the prevalence of pterygium was significantly associated with increasing age, which is similar to almost all epidemiologic studies on different ethnicities.<sup>[6,9,24]</sup> Early modification of risk factors is immensely relevant for the older population since pterygium could result in significant astigmatism and visual impairment, which may affect their visual function, lifestyle, and productivity.

**Table 1. Demographic data of patients in cases and controls**

	Total	Group		P
		Case	Control	
Age				
Mean±SD	46.4±18.4	50.8±14.8	41.9±20.4	<0.001 <sup>†</sup>
<40	146 (34.8%)	58 (27.6%)	88 (41.9%)	
>40	274 (65.2%)	152 (72.4%)	122 (58.1%)	
Sex				
Male	223 (53.1%)	128 (61.0%)	95 (45.2%)	0.001*
Ultra violet exposure				
Mean±SD	8±6	7±6	8±6	0.606 <sup>‡</sup>
Occupation				
Other	75 (17.9%)	47 (22.4%)	28 (13.3%)	<0.001*
Housewife	153 (36.4%)	70 (33.3%)	83 (39.5%)	
Clerk	56 (13.3%)	29 (13.8%)	27 (12.9%)	
Student	52 (12.4%)	5 (2.4%)	47 (22.4%)	
Farmer	59 (14.0%)	46 (21.9%)	13 (6.2%)	
Manual Laborer	25 (6.0%)	13 (6.2%)	12 (5.7%)	
Residential area				
Education				
Rural	199 (47.4%)	88 (41.9%)	111 (52.9%)	0.025*
Illiterate	102 (24.3%)	45 (21.4%)	57 (27.1%)	0.791 <sup>‡</sup>
<12	182 (43.3%)	102 (48.6%)	80 (38.1%)	
12	66 (15.7%)	36 (17.1%)	30 (14.3%)	
Bakery	114 (27.1%)	114 (54.3%)	0 (0.0%)	<0.001*
Family history	57 (13.6%)	48 (22.9%)	9 (4.3%)	<0.001*
Cigarette smoking	96 (22.9%)	80 (38.1%)	16 (7.6%)	<0.001*
Blepharitis	24 (5.7%)	22 (10.5%)	2 (1.0%)	<0.001*
Dry eye	81 (19.3%)	62 (29.5%)	19 (9.0%)	<0.001*
Hypertension	123 (29.3%)	81 (38.6%)	42 (20.0%)	<0.001*
Ischemic heart disease	50 (11.9%)	40 (19.0%)	10 (4.8%)	<0.001*
Obesity	52 (12.4%)	33 (15.7%)	19 (9.0%)	0.038*

\*Based on Chi-Square test.<sup>†</sup>Based on *t*-test.<sup>‡</sup>Based on Mann-Whitney test

The evidence on the role of sex in the pathogenesis of pterygium is contradictory; some studies reported a higher prevalence in one sex, but others failed to find the association.<sup>[6,25-27]</sup> In univariate analysis, we found a higher prevalence of pterygium in male patients, but it was not significant in multivariate analysis. It seems that the role of sex is relevant in the social and professional context; once it is corrected for these parameters, it is no longer a risk factor.

There is no consensus regarding the pathogenesis of pterygia, but epidemiological evidence strongly supports its association with other sun-related disorders and validates the concept that ultraviolet radiation plays a major role in the development of pterygium.<sup>[2]</sup>

Sun exposure is implicated as a risk factor in low altitude, primary residential area, occupation, and current habits of population.

In agreement with previous studies, outdoor work (farmers) and residence in rural area were significantly associated with higher prevalence of pterygia.<sup>[28,29]</sup>

The association between low education and prevalence of pterygium is a matter of debate. While some investigators found statistically significant association between lower levels of education and pterygia, others failed to prove the connection.<sup>[27,28,30]</sup> In the present study, we did not find lower educational level to be associated with higher prevalence of pterygium.

There was a significant association between pterygium and cigarette smoking in our study. Cigarette smoking is one of the most common lifestyle-related exposures, and recently has been linked to the occurrence of pterygium.<sup>[26]</sup> The association between smoking and pterygium is inconsistent among studies, most probably due to selection bias.<sup>[28]</sup> Using a systematic approach, Rong et al, summarized the association between smoking and pterygium, and showed that cigarette smoking had a protective effect against pterygium with pooled odds ratio of 0.82 and 95% confidence interval (0.69 to 0.97).<sup>[31]</sup> In contrast to the findings of Rong et al, we found that cigarette smoking was a risk factor in the

**Table 2. Significance of the risk factors based on multivariate analysis**

	AOR	95% CI		P
		Lower	Upper	
Age				
>40	0.74	0.35	1.56	0.023
<40	1.00			
Sex				
M	1.43	0.46	4.51	0.537
F	1.00			
Occupation				
Other	1.11	0.35	3.55	0.861
Housewife	0.49	0.10	2.43	0.385
Clerk	0.72	0.19	2.69	0.620
Student	0.06	0.01	0.33	0.001
Farmer	3.84	1.01	14.67	0.049
Manual Laborer	1.00			
Residential area				
area				
Rural	1.39	0.75	2.59	0.300
Urban	1.00			
Education*				
Illiterate	0.37	0.11	1.22	0.103
<12	1.70	0.67	4.33	0.267
12	1.45	0.59	3.59	0.422
Family history	9.59	3.43	26.84	<0.001
Cigarette smoking	5.46	2.65	11.27	<0.001
Bakery*	4.27	1.71	10.62	0.002
Blepharitis*	23.86	3.13	181.82	0.002
Dry eye*	2.50	1.19	5.28	0.016
Ultra violet exposure	0.62	0.27	1.43	0.260

AOR, adjusted Odds ratio represents the simultaneous effect of all variables, based on multiple logistic regression; \*Remained in the model with backward likelihood ratio selection method

case group. Their observational study may have selection bias, which limits the ability of making a convincing conclusion. There is also an undetermined dose-response relationship between smoking and the risk of pterygium. The biological pathways that link cigarette smoking with risk reduction are not well understood, and until more compelling evidence is available, it is hard to draw concrete conclusions based on current observational studies.

Family history of pterygium was found to have a significant association with increased prevalence of pterygium in the current study. Hereditary predisposition to pterygium development has not been highlighted in other studies. Several modes of inheritance have been reported such as autosomal dominant, autosomal recessive, sex linked, and non-Mendelian modes of inheritance.<sup>[32]</sup> However, current studies rely on self-reported data, which may be biased. Thus, larger studies are needed to increase cogency.

We also found higher prevalence of pterygium among those with a history of bread baking, which has not been reported before. Baking in its traditional form in rural areas is accompanied by high levels of smoke exposure and dry conditions. Both of these are associated with inflammation and interfere with normal tissue repair. Inflammation and repetitive micro trauma have been proposed as possible causes of pterygium.<sup>[2]</sup>

Blepharitis was associated with higher risk of pterygia in our study. Although the role of blepharitis has not been reported in literature, an inflammatory reaction is a well-established pathogenesis of pterygium. We hypothesize that blepharitis induced inflammation, which increased the number of reactive oxygen species that play a role in phosphorylation of the cell membrane and increased the products of lipid metabolism.<sup>[32]</sup> Inflammatory cells are present in all pterygium samples, which indicates inflammation as a causative step in pterygium development.<sup>[19]</sup>

Ilam province is located in the west of Iran, with dry and hot weather. It is dusty for most days of the year in this province. Dust is a known risk factor for pterygium development,<sup>[16]</sup> which explains the high prevalence of pterygium in spite of the high altitude of the region.

Compared to previous studies, this study reports more risk factors related to the prevalence of pterygium. It also found blepharitis and baking as previously undetected risk factors and confirmed the already established risk factors.

In conclusion, health system plans and strategies should target the dusty and polluted environment of Ilam province to decrease the prevalence of pterygium. Since limiting sun exposure has proven protective effect against pterygium development, the enhancement of cultural acceptance of sunglasses and brimmed hats could effectively reduce the prevalence of pterygium and related visual impairments.

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## Conflicts of Interest

There are no conflicts of interest.

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