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# Rate of allergic disorders and skin prick sensitivity to common allergens among patients suffering from pterygium in Birjand, Iran

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# 翼状胬肉患者中过敏性疾病和常见过敏源皮肤 针刺试验阳性率

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# 摘要

**目的:**评估翼状胬肉患者中过敏性疾病流行情况和皮肤针刺试验阳性率。

方法:62 例翼状胬肉患者与年龄性别匹配的相同数量健康受试者纳入了这项研究。所有患者和健康受试者均接受眼科医生和过敏性疾病专科医生检查。皮肤针刺试验检测了常见致敏原。血清总 IgE 使用 ELISA 检测。

结果:过敏性鼻结膜炎在翼状胬肉患者中更多(19.3% vs 3.2%, P=0.002),但是在其他过敏性疾病或过敏症状上的差异没有统计学意义。皮肤针刺试验中,翼状胬肉患者对至少一种致敏原阳性的比率显著高于健康人(38.7% vs 6.5%, P=0.003)。蟑螂和尘螨是所调查翼状胬肉患者中最常见的致敏原(16.1%、12.9%)。

**结论:**本研究发现翼状胬肉患者中鼻结膜炎和皮肤针刺试验阳性率均较正常人高。

关键词:过敏;过敏症;翼状胬肉

# Abstract

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• AIM: To evaluate the prevalence of allergic disorders and skin prick test sensitivity to different allergens among patients with pterygium.

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- METHODS: Sixty two patients with pterygium and equal number of age/ sex matched healthy controls were enrolled in this study. All patients and controls examined by an ophthalmologist and allergist. Skin prick test performed with a battery of common allergens and serum total IgE level determined by ELISA method.
- RESULTS: Prevalence of allergic rhinoconjunctivitis was significantly higher in patient group (19.3% vs 3.2%, P= 0.002) but there was no significant differences in other allergies and symptoms between two groups. The rate of skin reactivity to at least one allergen was significantly higher in pterygium group than healthy controls (38.7% vs 6.5%, P= 0.003). Cockroach and house dust mites were the most prevalent allergens among patients (16.1% and 12.9%).
- CONCLUSION: The results of current study showed higher prevalence of rhinoconjunctivits and skin prick sensitivity to allergen among pterygium patients. This may has implication in prevention and treatment of pterygium.
- KEYWORDS: allergy; hypersensitivity; pterygium DOI:10.3980/j.issn.1672-5123.2018.9.03

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## INTRODUCTION

P terygium is a common and benign condition of the eye which characterizes by fibrovascular spreading of conjunctiva to the cornea. It causes dryness, itching, redness or burning of the eye and in the larger forms can affect patient's vision<sup>[1]</sup>. The incidence of pterygium is varied in

Table 1 Prevalence of allergies and allergy related symptoms in pterygium patients and healthy controls

Symptoms	Pterygium patients (%)	Healthy controls (%)	P
Wheezing	4(12.9)	1(3.2)	0.14
Shortness of breath	7(22.6)	1(3.2)	0.01
Cough	2(6.5)	0(0)	0.09
Sneezing	8(25.8)	7(22.6)	0.76
Runny nose	7(22.6)	5(16.1)	0.52
Eye itching	8(25.8)	7(22.6)	0.76
Skin pruritus	1(3.2)	2(6.5)	0.55
Asthma	2(6.5)	0(0)	0.09
Eczema	2(6.5)	1(3.2)	0.55
Allergic rhinoconjunctivitis	6(19.3)	1(3.2)	0.03

different parts of the world but is higher in hot and dry areas and mostly affects people aged  $20-40y^{[2]}$ . From the pathologic point of view, limbal epithelial cell metaplasia to goblet cell, neovascularization and accumulation of fibroblasts as well as inflammatory cells in extra-cellular matrix can be seen frequently<sup>[3-5]</sup>. Although the underlying mechanism of pterygium is not well understood, many studies identified several predisposing factors including sunlight, dry eyes, dust, smoke, male sex and even inheritance<sup>[6-11]</sup>.

In molecular level, mutation of tumor controlling genes such as P-53 and  $P-63^{[12]}$ , growth factors like basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF) [13-14], progenitor cells [15-16] as well as infection with human papillomavirus[17-18] is considered to have a role in pathogenesis of pterygium. There are also some reports about the role of different immune mechanisms in pathogenesis of pterygium<sup>[19]</sup>. Accumulation of T cells, B cells in pterygium or depositions of different classes of antibodies are reported by several researches[19-25]. A few old studies have shown the presence of mast cells [26-30] and IgE in ptervgium that may suggest a role for type 1 hypersensitivity reaction in pterygium<sup>[21, 31]</sup>. Give the role of immune system particularly mast cells and IgE in pterygium and the potential role of exposure to environmental allergens in pathogenesis of pterygium as well as the lack of studies in this field, the aim of this study was to compare the prevalence of allergies and skin sensitivity to common allergens between patients suffering from pterygium and healthy controls. We hope that the results of the current study shed a light on pathogenesis of pterygium and help better management of this disease.

## SUBJECTS AND METHODS

Sixty two patients with pterygium and equal number of age and sex matched healthy cases without pterygium that referred to Eye Clinic of Vali – Asr Hospital enrolled in this study. Patients and controls were examined carefully by an expert ophthalmologist and those who had any serious illness such as cancer, autoimmune disorders or receive any drugs were excluded from this study. The study was approved by the

Ethics Committee of the Birjand University of Medical Sciences and all participants provided written informed consent before enrolling in the study. Data about demographic variables, history of eye diseases and allergic related symptoms were obtained by a questionnaire.

Skin Pricks Testing Skin prick tests (SPT) was performed by an allergist with a battery of 12 common regional allergen extracts (HollisterStier, USA) including grass mix, weeds mix, tree mix, mold mix, cockroach mix, mite mix, melon and orange. Histamine hydrochloride (10 mg/mL) and glycerol saline as positive and negative controls were respectively used. The mean wheal size was recorded after 15min and SPT was regarded as positive with a wheal size of minimum 3-mm larger than the negative control. Three patients were excluded from the study because of anti-histamine drug usage or a positive response to negative control.

**Total IgE Measurement** Five milliliters of venous blood was collected from all participants and after serum separation, the level of total IgE was measured by a commercial ELISA kit (Radim, Italy) in duplicate. Based on the manufacturer's instructions, IgE level of higher than 160 IU/mL was considered as high total IgE.

**Statistical Analysis** Data were analyzed by SPSS software package version 16 (Chicago, USA). Chi-squared test or Fisher exact test were used for comparison of frequencies. Total IgE is presented as geometric mean with 95 % confidence interval. *P* value less than 0.05 was considered significant.

## **RESULTS**

Sixty two patients with pterygium (mean age =  $46.5 \pm 16$ y, M/F ratio = 1.8/1) and equal number of healthy controls (mean age =  $40.1 \pm 9.7$ y, M/F ration = 1.8/1) participated in this study. There was no significant difference in age or sex between two groups. The prevalence of allergic rhinoconjunctivitis was significantly higher in patients group than controls (19.3% vs 3.2%, P = 0.002) but for other allergies and related symptoms the frequency was higher in pterygium patients although not significant (Table 1).

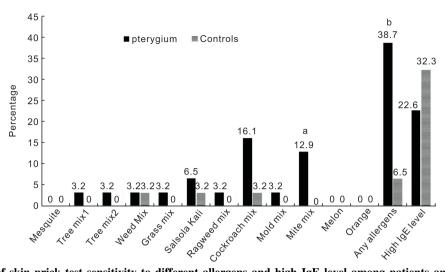


Figure 1 Frequency of skin prick test sensitivity to different allergens and high IgE level among patients and controls  ${}^aP = 0.016$  compared with control group;  ${}^bP = 0.003$  compared with control group.

Prevalence of skin sensitivity to most of extracts was higher in patient group but the difference was significant just for mite extract (12.9% vs 0, P = 0.016) (Figure 1). There were 38.7% of patients and 6.5% of controls showed skin sensitivity to at least one allergenic extracts (P=0.003). Although the meanserum IgE level was higher in patients group but not significant (121.9±142 IU vs 108.4±98 IU). In contrast prevalence of high serum IgE level was higher in controls than patients although not significant (32.3% vs 22.6%).

#### **DISCUSSION**

The aim of present study was to evaluate the possible role of allergy in pathogenesis of pterygium. Our results confirmed higher prevalence of allergic rhinoconjunctivitis and skin prick sensitivity in patients with pterygium than controls. Although several studies demonstrated the role of immunology in pterygium the documents about the role of allergy in pterygium are fairly scarce. Ang et  $al^{[32]}$  and his colleagues as well as Nangia et  $al^{[33]}$  found a positive correlation between acute pterygium and working in open environment due to exposure to sunlight, dust and possibly aeroallergens. Liu<sup>[19]</sup> and Gierek et  $al^{[31]}$  suggested a role for immunologic reactions mainly type 1, 3 and 4 in pathogenesis of pterygium.

In this regard Pinkerton et al<sup>[34]</sup> showed deposition of IgE antibody in all studied pterygium samples which are somehow consistent with our results as allergic rhinoconjunctivitis and skin prick test sensitivity both mediated by IgE and therefore are of type 1 hypersensitivity. There are also several reports on the abundance of mast cells in pterygium which may support the role of allergic reaction in pterygium, considering the role of mast cells in allergic diseases. In the present study the average level of serum IgE was insignificantly higher in patients but the frequency of high serum IgE was higher among controls although not significant which may questioned the role of allergy in pterygium. Several studies introduced the concept

of "entopy" as a local allergic reaction without systemic presentation  $^{[35-36]}$ . In this regard, higher level of specific IgE in nasal polyp tissues than serum has reported and therefore measuring tissue IgE may be more informative rather than serum IgE  $^{[37]}$ . High prevalence of parasitic infections in our area that increases the average level of IgE and can mask the difference in our small patients group may explain this finding.

Rather than the rate of skin sensitivity and rhinoconjunctivitis which were significantly higher among patients than controls, the frequency of almost all other allergies or related symptoms was insignificantly higher in pterygium patients than healthy people<sup>[38]</sup>. Lack of significant difference between two groups may be explained by low accuracy and sensitivity of questionnaire-based evaluation particularly in elderly people with low education or by type II statistical error because of small sample size. To overcome this limitation, clinical evaluation and skin prick test as two more reliable methods performed by an allergist and a battery of common allergen extracts were used to increase the sensitivity of the test. Our results showed higher rate of skin sensitivity to most of allergens which reached to the significant level just for mites and somehow cockroach allergens. Based on data from allergic patients<sup>[39]</sup> and homes surveys<sup>[40-41]</sup> mites and cockroaches<sup>[42]</sup> are not prevalent allergens in our area but they are important in case of perennial allergic conjunctivitis (PAC) astheir allergens have proteolytic activity which cause damage to ocular epithelium<sup>[43]</sup>.

On the other hand, both allergens have year-round nature and the level of exposure is higher than seasonal allergens which result in chronic inflammation of conjunctiva. It is also worth mentioning the role of ocular allergy and use of antihistamines in eye dryness which is a known underlying factor for pterygium; support the possible role of allergy in development of pterygium<sup>[44-46]</sup>.

The results of current study for the first time showed that the prevalence of rhinoconjunctivitis and skin prick sensitivity to allergens was higher in pterygium patients. This could be indicative of a link between allergies and pterygium and might has implication in prevention and treatment of pterygium but more comprehensive studies are necessary.

#### REFERENCES

- 1 Coster D. Pterygium-an ophthalmic enigma. Br J Ophthalmol 1995;79 (4):304-305
- 2 Liu L, Wu J, Geng J, Yuan Z, Huang D. Geographical prevalence and risk factors for pterygium: a systematic review and Meta-analysis. *BMJ Open* 2013;3(11):e003787
- 3 Liu T, Liu Y, Xie L, He X, Bai J. Progress in the pathogenesis of pterygium. *Curr Eye Res* 2013;38(12):1191-1197
- 4 Todani A, Melki SA. Pterygium: current concepts in pathogenesis and treatment. *Int Ophthalmol Clin* 2009;49(1):21-30
- 5 Chui J, Di Girolamo N, Wakefield D, Coroneo MT. The pathogenesis of pterygium: current concepts and their therapeutic implications. *Ocul Surf* 2008;6(1):24-43
- 6 Pyo EY, Mun GH, Yoon KC. The prevalence and risk factors for pterygium in South Korea: the Korea National Health and Nutrition Examination Survey (KNHANES) 2009-2010. *Epidemiol Health* 2016; 38:e2016015
- 7 Tin SS, Wiwanitkti V. Risk factors for pterygium in the high-altitude communities. Nepal J Ophthalmol 2014;6(2):244
- 8 Rong SS, Peng Y, Liang YB, Cao D, Jhanji V. Does cigarette smoking alter the risk of pterygium? A systematic review and meta-analysis. *Invest Ophthalmol Vis Sci* 2014;55(10):6235-6243
- 9 Jiao W, Zhou C, Wang T, Yang S, Bi H, Liu L, Li Y, Wang L. Prevalence and risk factors for pterygium in rural older adults in Shandong province of China: a cross-sectional study. *Biomed Res Int* 2014;2014:658648
- 10 Taylor HR. Risk factors for pterygium. Ophthalmology 2013; 120
  (2):441
- 11 Young CH, Lo YL, Tsai YY, Shih TS, Lee H, Cheng YW. CYP1A1 gene polymorphisms as a risk factor for pterygium. *Mol Vis* 2010; 16: 1054-1058
- 12 Pelit A, Bal N, Akova YA, Demirhan B. p53 expression in pterygium in two climatic regions in Turkey. *Indian J Ophthalmol* 2009;57(3): 203-206
- 13 Nolan TM, DiGirolamo N, Sachdev NH, Hampartzoumian T, Coroneo MT, Wakefield D. The role of ultraviolet irradiation and heparin-binding epidermal growth factor like growth factor in the pathogenesis of pterygium. *Am J Pathol* 2003;162(2):567–574
- 14 Bianchi E, Scarinci F, Grande C, Plateroti R, Plateroti P, Plateroti AM, Fumagalli L, Capozzi P, Feher J, Artico M. Immunohistochemical profile of VEGF, TGF-beta and PGE<sub>2</sub> in human pterygium and normal conjunctiva: experimental study and review of the literature. *Int J Immunopathol Pharmacol* 2012;25(3):607-615
- 15 Lee JK, Song YS, Ha HS, Park JH, Kim MK, Park AJ, Kim JC. Endothelial progenitor cells in pterygium pathogenesis. *Eye* (*Lond*) 2007;21(9):1186-1193
- 16 Ye J, Song YS, Kang SH, Yao K, Kim JC. Involvement of bone marrow derived stem and progenitor cells in the pathogenesis of pterygium. *Eye* (*Lond*) 2004;18(8):839–843
- 17 Chalkia AK, Spandidos DA, Detorakis ET. Viral involvement in the

- pathogenesis and clinical features of ophthalmic pterygium (Review). *Int J Mol Med* 2013;32(3):539-543
- 18 Sjo NC, von Buchwald C, Prause JU, Norrild B, Vinding T, Heegaard S. Human papillomavirus and pterygium. Is the virus a risk factor? *Br J Ophthalmol* 2007;91(8):1016–1018
- 19 Liu L, Yang D. Immunological studies on the pathogenesis of pterygium. *Chin Med Sci J* 1993;8(2):84-88
- 20 Solomon AS. Immunologic basis for the pathogenesis of pterygium. Am J Ophthalmol 1985;99(2):216-217
- 21 Pinkerton OD, Hokama Y, Shigemura LA. Immunologic basis for the pathogenesis of pterygium. *Am J Ophthalmol* 1984;98(2):225-228
- 22 Golu T, Mogoanta L, Streba CT, Pirici DN, Malaescu D, Mateescu GO, Muţiu G. Pterygium: histological and immunohistochemical aspects. *Rom J Morphol Embryol* 2011;52(1):153-158
- 23 Beden U, Irkec M, Orhan D, Orhan M. The roles of T-lymphocyte subpopulations (CD4 and CD8), intercellular adhesion molecule 1 (ICAM-1), HLA-DR receptor, and mast cells in etiopathogenesis of ptervgium. *Ocul Immunol Inflamm* 2003;11(2):115-122
- 24 Tekelioglu Y, Turk A, Avunduk AM, Yulug E. Flow cytometrical analysis of adhesion molecules, T lymphocyte subpopulations and inflammatory markers in pterygium. *Ophthalmologica* 2006; 220 (6): 372–378
- 25 Awdeh RM, DeStafeno JJ, Blackmon DM, Cummings TJ, Kim T. The presence of T-lymphocyte subpopulations (CD4 and CD8) in pterygia: evaluation of the inflammatory response. *Adv Ther* 2008; 25 (5):479-487
- 26 Liang K, Jiang Z, Zhao B, Shen J, Huang D, Tao L. The expression of vascular endothelial growth factor in mast cells promotes the neovascularisation of human pterygia. *Br J Ophthalmol* 2012;96(9): 1246–1251
- 27 Celebi AR, Ozbey C, Mirza GE. The role of mast cells in vascularized recurrent pterygium. *Arq Bras Oftalmol* 2014; 77 (5): 285–287
- 28 Nakagami T, Murakami A, Okisaka S, Ebihara N. Mast cells in pterygium: number and phenotype. *Jpn J Ophthalmol* 1999; 43 (2): 75–79
- 29 Ratnakar KS, Goswamy V, Agarwal LP. Mast cells and pterygium. Acta Ophthalmol (Copenh) 1976;54(3):363-368
- 30 Ribatti D, Nico B, Maxia C, Longo V, Murtas D, Mangieri D, Perra MT, De Giorgis M, Piras F, Crivellato E, Sirigu P. Neovascularization and mast cells with tryptase activity increase simultaneously in human pterygium. *J Cell Mol Med* 2007;11(3):585–589
- 31 Gierek-Lapinska A, Lange E, Mrukwa-Kominek E, Gierek-Ciaciura S. Pterygium; allergic etiology? *Pol Merkur Lekarski* 2003;14(84):718
- 32 Ang M, Li X, Wong W, Zheng Y, Chua D, Rahman A, Saw SM, Tan DT, Wong TY. Prevalence of and racial differences in pterygium; a multiethnic population study in Asians. *Ophthalmology* 2012;119 (8): 1509-1515
- 33 Nangia V, Jonas JB, Nair D, Saini N, Nangia P, Panda-Jonas S. Prevalence and associated factors for pterygium in rural agrarian central India. The central India eye and medical study. *PLoS One* 2013;8(12): e82439
- 34 Pinkerton OD, Hokama Y, Shigemura LA, Immunologic basis for the pathogenesis of pterygium. *Am J Ophthalmol* 1984;98(2):225-228
- 35 Forester JP, Calabria CW. Local production of IgE in the respiratory mucosa and the concept of entopy: does allergy exist in nonallergic rhinitis? *Ann Allergy Asthma Immunol* 2010; 105 (4): 249 55; quiz 56–58
- 36 Powe DG, Bonnin AJ, Jones NS. 'Entopy': local allergy paradigm. Clin Exp Allergy 2010;40(7):987-997

- 37 Bakhshaee M, Fereidouni M, Nourollahian M, Movahed R. The presence of fungal specific IgE in serum and sinonasal tissue among patients with sinonasal polyposis. *Eur Arch Otorhinolaryngol* 2014; 271 (11):2871–2875
- 38 Fereidouni M, Abolhasani A, Vahedi F, Shakeri MT, Varasteh A. A preliminary survey of the prevalence of allergic disorders in a questionnaire-based study in Boshroye, a rural area of Iran. *Journal of Public Health* 2010;18(2);2
- 39 Fereidouni M, Hossini RF, Azad FJ, Assarehzadegan MA, Varasteh A. Skin prick test reactivity to common aeroallergens among allergic rhinitis patients in Iran. *Allergol Immunopathol (Madr)* 2009;37(2):73–79
- 40 Fereidouni M, Fereidouni F, Hadian M, Nourani Hasankiadeh S, Mazandarani M, Ziaee M. Evaluation of the level of house dust mite allergens, Der p 1 and Der f 1 in Iranian homes, a nationwide study. *Allergol Immunopathol (Madr)* 2013;41(6):381–386
- 41 Fereidouni M, Fereidouni F, Hadian M, Asghari Z, Zojaji SM. The level of mite dermatophagoides' allergens (Der-p 1 and Der-f 1) in

- Birjand. Zahedan J Res Med Sci (ZJRMS) 2014;16(4):38-40
- 42 Moghtaderi M, Farjadian S, Fereidouni M, Nasiri M, Nejat A. Indoor dust allergen levels in the homes of patients with childhood asthma; an experience from Southwestern Iran. *Iran J Allergy Asthma Immunol* 2016;15(2):132–137
- 43 Chapman MD, Wunschmann S, Pomes A. Proteases as Th2 adjuvants. *Curr Allergy Asthma Rep* 2007;7(5):363-367
- 44 Hom MM, Nguyen AL, Bielory L. Allergic conjunctivitis and dry eye syndrome. *Ann Allergy Asthma Immunol* 2012;108(3):163-616
- 45 Ousler GW, Wilcox KA, Gupta G, Abelson MB. An evaluation of the ocular drying effects of 2 systemic antihistamines: loratadine and cetirizine hydrochloride. *Ann Allergy Asthma Immunol* 2004; 93 (5): 460–464
- 46 Ousler GW, 3rd, Workman DA, Torkildsen GL. An open-label, investigator-masked, crossover study of the ocular drying effects of two antihistamines, topical epinastine and systemic loratadine, in adult volunteers with seasonal allergic conjunctivitis. *Clin Ther* 2007;29(4):611-616