# Ocular exposure to particulate matter and pterygium: a case-control study

## Authors

Carlos Alberto Ramirez (1)

Manuel Pérez-Martinot (2)

Delia Gil-Huayanay (3)

Diego Urrunaga-Pastor (4)

Vicente A. Benites-Zapata (4)

# Affiliation

1 Escuela de Posgrado, Universidad ESAN, Lima, Perú.

2 Facultad de Medicina, Universidad Peruana Cayetano Heredia, Lima, Perú.

3 Facultad de Medicina, Universidad de San Martín de Porres, Lima, Perú.

4 Vicerrectorado de Investigación, Universidad San Ignacio de Loyola, Lima, Perú

Short running title: Particulate matter and pterygium.

#### Mails

Carlos Alberto Ramirez

Manuel Pérez-Martinot

Delia Gil-Huayanay

Diego Urrunaga-Pastor

Vicente A. Benites-Zapata

cramirezlt@gmail.com

drmperezm@gmail.com

delia.gil.h@gmail.com

diego.urrunaga.pastor1@gmail.com

vbeniteszapata@gmail.com

# **Corresponding author**

Vicente A. Benites-Zapata

Address: Av. la Fontana 750, Lima 15024

Mail: vbeniteszapata@gmail.com

Phone: +51995523081

# Funding

Self-funded.

# **Conflict of interest**

The authors disclose no conflict of interest.

#### Abstract

**Background:** Pterygium formation has been mainly associated to ultraviolet (UV) radiation exposure. However, other factors such as dry weather, wind exposure and microtrauma with dust particles have been linked to pterygium development.

**Objective:** To determine the association between ocular exposure to particulate matter and pterygium.

**Methods:** We used a case-control design, with cases identified in November 2013. This study was conducted in a company dedicated to the production and marketing of toilets. We included a total of 90 cases and 184 controls. The diagnosis of the pterygium was performed by clinical evaluation and we included variables as age and working time in the company. We performed logistic regression models (crude and adjusted) to assess the proposed association. The reported association measure was the Odds Ratio (OR) with their respective 95% confidence intervals (95% CI).

**Results:** All the participants were male; the mean age of the cases was  $39.9 \pm 9.5$  years, while the mean age of the controls was  $37.8 \pm 7.3$  years. Then, 42% (n=115) of the participants was working in the company for 5-8 years. The prevalence of ocular exposure to particulate matter among the study participants was 31% (n=84). In addition, the percentages of cases and controls exposed to particulate matter were of 31.1% (n=28) and 30.4% (n=56), respectively. In the adjusted logistic regression model, the association remained with no statistical significance (OR=1.08; 95%CI: 0.61-1.91).

**Conclusions:** We did not find association between ocular exposure to particulate matter and pterygium development in the study population.

**Keywords:** Pterigyum; Particulate matter; Dust; Occupational Exposure; Occupational Medicine; Adult (Source: MeSH NLM).

## Take-home messages

- We did not find association between ocular exposure to particulate matter and pterygium formation in workers of a factory dedicated to production and commercialization of toilets and ceramics.
- 2. In our study, we empirically measured the ocular exposure to particulate matter, nevertheless, it is necessary to validate a standardized methodology to quantify this parameter.
- 3. We suggest to perform multicentre case-control and cohort studies to validate the findings of this investigation.

#### 1. Introduction

Pterygium is an important consultation reason in ophthalmological health care and is one of the most common eye diseases.<sup>1-3</sup> It is considered an inflammatory process associated with cell proliferation, connective tissue remodelling and angiogenesis; leading to fibrovascular proliferation.<sup>4,5</sup>

Pterygium formation has been linked to several factors. Exposure to ultraviolet (UV) radiation is described as the most relevant risk factor; however, other associated factors have been also mentioned, such as dry weather, dust, rapid evaporation of the tear film, genetic transmission, ametropia, exposure to wind and microtrauma with dust particles, and even exposure to harmful chemicals.<sup>6-17</sup> Nevertheless, there is no consensus regarding the influence of these factors in the pterygium pathogenesis.<sup>18</sup>

In mild and non-inflamed cases, the pterygium is usually asymptomatic.<sup>19-22</sup> However, in advanced or recurrent forms, elevated areas can cause symptomatic epithelial keratopathy, producing tearing reflex, photophobia and foreign body sensation.<sup>2,3,23,24</sup> If it grows, it can reduce the visual capacity, causing irregular astigmatism.<sup>2,22,24</sup>

The diagnosis is based in clinical findings after a careful ophthalmological exploration of the patient, trying to locate pathogenic activity, such as a fibrous and vascular proliferation on the conjunctiva (unilateral or bilateral) that contains blood vessels arranged radially in relation to the eye vertex.<sup>25</sup>

The company where the study was developed has more than 50 years of existence and is dedicated to the production and marketing of toilets and ceramics. Part of their productive activities generate particulate matter, for example, in the preparation of the plaster, the preparation of the frit, the polishing and enamelling of the sanitary ware. These activities were carried out in roofed spaces with no solar radiation exposure, however, the workers did not have eye protection. Therefore, the ocular conjunctiva of the operators was in contact with the particulate matter. Thus, this study aimed to determine the association between ocular exposure to particulate matter and pterygium formation in workers of a factory dedicated to production and commercialization of toilets and ceramics.

## 2. Material and Methods

## 2.1. Study design

This is an observational and analytical study, with a case and control design.

## 2.2. Population, sample type and sample

The study was carried out in November 2013. The company, where the study was developed, had 1301 workers and is dedicated to the production and marketing of toilets.

The sample type was non-probabilistic. We conducted a pilot study including 11 cases and 22 controls from the evaluated population, considering the same inclusion and exclusion criteria of the final sample. Thus, the sample size was calculated using an estimated Odds Ratio (OR) of 2.5 and a case exposure frequency of 27% (which was obtained through the pilot study), a statistical power of 80%, a confidence level of 95%, and a case-control ratio of 1:2; obtaining a minimum necessary sample of 90 cases and 180 controls. This was calculated with the statistical software EPIDAT 4.0 elaborated by the World Health Organization (WHO).

# 2.3. Procedures

As part of the production process, some work activities generated particulate matter, for example: the polishing and enamelling of the toilets. These activities were carried out with no sunlight exposure or ocular protection. The polishing and enamelling activities conducted the operators to finish their work routine with the upper two-thirds of the face covered with particulate matter, despite using the face respirator and the wimple.

For this reason, the company carried out an occupational medical campaign of 5 days during November 2013. The doctor in charge of this activity identified the pterygium cases for this study and we reviewed their occupational medical examinations.

2.4. Case definition

Workers diagnosed with pterygium, with 5 or more years working in a company environment with dosimetries values higher than 10 mg/m<sup>3</sup> for total/inhalable dust and 3 mg/m<sup>3</sup> for respirable dust.

2.5. Control definition

Workers with no diagnosis of pterygium, with 5 or more years working in a company environment with dosimetries values higher than 10 mg/m<sup>3</sup> for total/inhalable dust and 3 mg/m<sup>3</sup> for respirable dust.

2.6. Elegibility criteria

We excluded workers with a family history of pterygium, daily consumption of alcohol greater than 40g of ethanol,<sup>26,27</sup> moderate smokers (6 to 15 cigarettes per day).<sup>11,28,29</sup> Similarly, people who worked in not covered areas and therefore, they were more exposed to UV radiation during the execution of their activities. Additionally, workers who previously laboured in fishing, masonry, public transportation, construction and agriculture were excluded, as this are jobs exposed to higher UV radiation levels of UV than other occupational groups.

Equally, we excluded people who worked in environments that had high thermal stress and low relative humidity; both risk factors for the development of pterygium.

To identify this environments, we reviewed the measurements of the work areas based on the Wet Bulb Globe Temperature Index (WBGT, ISO 7243, 1989). The limit values of WBGT were established according to the American Conference on Governmental Industrial Hygienists (ACGIH) of 2012, by using Quest Technologies equipment, model QUESTEMP 36 and series TKI090009.

#### 2.7. Variables definition

#### 2.7.1. Outcome

The main variable of the study was the presence of pterygium in the participants. This was determined by reviewing the occupational medical examinations of the identified cases during the company medical campaign in November 2013.

#### 2.7.2. Exposure

We defined ocular exposure to particulate matter if the participant had 5 or more years working in an environment with dosimetries values higher than 10 mg/m<sup>3</sup> for total/inhalable dust and 3 mg/m<sup>3</sup> for respirable dust. According to these criteria, the jobs that fulfilled the definition were the polishing, enamelling, kilns and frit operators.

To objectify the ocular exposure to particulate matter, we had access to occupational hygiene monitoring and to the total, inhalable and respirable dust dosimetries, carried out in the company during the last 5 years prior the study. These measurements were performed with calibrated dosimeters, certified and operated by environmental engineers with a minimum experience of three years in occupational hygiene monitoring.

We applied the 0500 and 0600 methodologies of the National Institute for Occupational Safety and Health (NIOSH) for the quantification of total, inhalable and respirable dust. Moreover, the maximum permissible values were established according to the ACGIH of 2012. We used calibrated constant flow pumps of Sensidyne brand and BDX II model to collect the air samples. Furthermore, we append photos of the evaluated company staff during their work activities and at the end of them (Figure 1).

2.7.3. Other variables

Additionally, other variables such as age (years) and working time in the company (years) were collected. The age (years) of the participants was categorized in four groups: <33, 33-37, 38-42 and >42. The working time in the company was categorized into: 5-8, 9-12 and >12.

2.8. Statistical analysis

We used the statistical package STATA v12.0 (Statacorp, Tx, USA) to perform the analysis. The descriptive results for numeric variables were presented as means with standard deviation (SD), and the qualitative variables were expressed as numbers with percentages. The participants characteristics according to pterygium presence or not, were compared using the Chi square test.

We performed logistic regression models (crude and adjusted), the estimated association measure was the OR with their respective 95% confidence intervals (95% CI). The adjusted model included the following variables: age (years) and working time in the company (years).

Additionally, we assessed the statistical interaction between the participants age (categorized in quartiles) and the ocular exposure to particulate matter. The interaction term was created by multiplying the age quartiles with the ocular exposure to particulate matter. We evaluated the statistical interaction using the Mantel-Haenszel test<sup>30</sup> with a significance determined by a p-value <0.05.

2.9. Ethical issues

The study protocol was reviewed and approved by Institutional Review Boards at Universidad Peruana Cayetano Heredia, in Lima, Peru.

#### 3. Results

A total of 90 cases and 184 controls were included in the study. All the participants were male, the mean age of the cases was 39.9 years  $\pm$  9.5 (SD), while the mean age of the controls was 37.8 years  $\pm$  7.3 (SD); however, this difference was not statistically significant (p=0.28). Then, 42% (n=115) of the participants was working in the company for 5-8 years (Table 1).

The prevalence of ocular exposure to particulate matter among the study participants was 31% (n=84). In addition, the percentages of cases and controls exposed to particulate matter were of 31.1% (n=28) and 30.4% (n=56), respectively; however, this was not statistically significant (p=0.91). Moreover, we did not observe statistically significant differences between the cases and controls, regarding the age groups (p=0.26). Similarly, we did not find statistically significant differences between cases and controls, in relation to the working time in the company (p=0.75) (Table 1).

In the crude logistic regression model, we found that ocular exposure to particulate matter was not associated with the presence of pterygium in this population group (OR=1.03; 95%CI: 0.60-1.78). Equally, in the adjusted model, the association remained with no statistical significance (OR=1.08; 95%CI: 0.61-1.91) (Table 2).

Finally, in the logistic regression model with the multiplicative interaction term, we did not find a statistically significant association between age quartiles and ocular exposure to particulate matter, with the pterygium presence.

#### 4. Discussion

In the present study, we did not find association between ocular exposure to particulate matter and the presence of pterygium. A study carried out in Nigeria with 144 motorcyclists and a control group of 114 office workers from the same company, aimed to determine the risk factors associated with the pterygium development. The authors reported that there was no association between working time as a motorcyclist and the presence of pterygium. In addition, the use of sunglasses and hats was related with a protective effect for the pterygium formation.<sup>25</sup> In contrast, another study also conducted in Nigeria with 615 motorcyclists, found no association between the use of sunglasses and the prevalence of pterygium.<sup>31</sup>

Furthermore, in a cross-sectional study conducted in 553 sawmill workers in Nigeria, of whom 449 and 104 performed technical and administrative tasks, respectively; it was found that a worker with technical tasks had more than twice of probabilities to develop pterygium compared to a sawmill administrative worker. Nevertheless, they did not perform a regression analysis adjusted for potential confounders as in our study.<sup>32</sup> Moreover, a high prevalence of pterygium has been reported in welders, however, these workers are exposed to smoke, whereas workers in our study were exposed to particulate matter.<sup>17</sup> However, in a Korean study conducted between 2006-2011 in 22 216 participants, it was found an association between exposure to particulate matter with aerodynamic diameter less than 10 μm and primary pterygium. This study also found a statistical association in the adjusted logistic regression model with the sun exposure, older age and less educational level in the participants.<sup>33</sup>

In the reviewed studies in different occupational groups, most agents related to particulate matter or dust do not describe a significant association with the pterygium formation. Nevertheless, some studies show that the use of hats and sunglasses (both) reduces the presence of pterygium.<sup>18,25</sup> These findings would elucidate that exposure to UV radiation could be the most important causal factor in the pterygium pathogenesis. Though to corroborate this hypothesis it is required to develop studies offering protection elements against UV radiation to the occupational groups with the highest risk of pterygium. Subsequently, it would be necessary to assess the impact of this intervention on the pterygium incidence.

In our study, the age of the participants was not associated with the pterygium development. Despite having evaluated the statistical interaction between ocular exposure to particulate matter and the age effect, there was no association with the presence of pterygium. However, pterygium prevalence has been linked with older age<sup>18,33</sup> and several studies has described a higher prevalence of this pathology among 20 and 50 years old.<sup>3,16,17,23</sup>

Regardless the negative result found in this study, it is important to consider eye protection measures when carrying out work activities in contact with particulate matter. This lack of association could be explained because the study population was under 40 years old and the risk of pterygium increases with age.<sup>18,33</sup> Thus, it is required prospective longitudinal studies with a follow-up of more than 10 years in order to determine whether exposure to particulate matter is a risk factor for the development of pterygium.

This study had certain limitations that must be mentioned: (1) the assessment of ocular exposure to particulate matter was performed through the measurement of total, inhalable and respirable dust. Unfortunately, in ophthalmological research, a validated criterion for this quantification has not vet been established. Despite this. we tried to objectify it, using the total/inhalable and respirable dust dosimetries performed with a validated methodology, trained personnel, calibrated and certified monitoring equipment. (2) Pterygium was not diagnosed by an ophthalmologist: however, it was done through the participation of a primary care physician. (3) The study was carried out in a single sanitary factory, so the findings cannot be extrapolated to this entire occupational group. Nevertheless, it was an advantage that both cases and the controls were selected from the same population. (4) We could not measure the degree of exposure to UV radiation, however, we excluded all workers who did not perform their activities below roof protection. Equally, we tried to control other important confounders, such as thermal stress and low relative humidity, excluding the participants who worked in areas with these conditions.

In conclusion, no association was found between ocular exposure to particulate matter and pterygium. We suggest to perform multicentre case-control and cohort studies to validate the findings of this investigation.

# 5. Tables and figures

Table 1. Characteristics of the study participants according to the presence of pterygium.

Variables	Cases (n=90)	Controls (n=184)	P value
Age (years)			0.26
<33	26 (28.9)	65 (35.3)	
33-37	26 (28.9)	37 (20.1)	
38-42	16 (17.8)	43 (23.4)	
>42	22 (24.4)	39 (21.2)	
Working time in the company (years)			0.75
5-8	38 (42.2)	77 (41.8)	
9-12	21 (23.3)	50 (27.2)	
>12	31 (34.5)	57 (31.0)	
Ocular exposure to particulate matter	4		0.91
No	62 (68.9)	128 (69.6)	
Yes	28 (31.1)	56 (30.4)	

Data expressed as number (percentage).

Table 2. Logistic regression analysis (crude and adjusted) to evaluate the association between ocular exposure to particulate matter and the presence of pterygium.

Variables	Crude OR (95%CI)	P value	Adjusted OR (95%CI)	P value
Ocular exposure to particulate matte	r			
No	Ref	-	Ref	-
Yes	1.03 (0.60-1.78)	0.90	1.08 (0.61-1.91)	0.79
Age (years)				
<33	Ref	-	Ref	-
33-37	1.75 (0.89-3.46)	0.10	1.80 (0.90-3.61)	0.10
38-42	0.93 (0.45-1.93)	0.84	0.86 (0.35-2.12)	0.75
>42	1.41 (0.70-2.82)	0.33	1.20 (0.44-3.26)	0.73
Working time in the company (years)	)			
5-8	Ref	-	Ref	-
9-12	0.85 (0.45-1.62)	0.62	0.82 (0.42-1.62)	0.58
>12	1.10 (0.61-1.98)	0.75	1.21 (0.50-2.95)	0.67

Figure 1. Photos of the company personnel during the execution and at the end of their activities.



Figure 1a: Polisher with particulate matter sampling pump. The white colour of the eyebrows is due to the dust generated by the polishing of the toilets.

Figure 1b: Enameller. The eyebrows and the ocular perimeter of white colour are caused by the particulate matter.

Figure 1c: Polisher with particulate matter sampling pump. The polishing booth is seen behind the employee.

Figure 1d: Enameller doing the lavatories enamelling process. The enamelling cabin and the mist generated are observed.

## 6. References

- 1. Rojas Álvarez E. Aspectos básicos del pterigion para médicos generales integrale. *Rev Cubana Med Gen Integr* 2009;**25:**127-37.
- 2. Luthra R, Nemesure BB, Wu S-Y, *et al.* Frequency and risk factors for pterygium in the Barbados Eye Study. *Arch Ophthalmol* 2001;**119:**1827-32.
- Wong TY, Foster PJ, Johnson GJ, et al. The prevalence and risk factors for pterygium in an adult Chinese population in Singapore: the Tanjong Pagar survey. Am J Ophthalmol 2001;131:176-83.
- 4. Kwok LS, Coroneo MT. A model for pterygium formation. Cornea 1994;13:219-24.
- 5. Coroneo M, Di Girolamo N, Wakefield D. The pathogenesis of pterygia. *Curr Opin Ophthalmol* 1999;**10:**282-8.
- 6. Kyei S, Owusu-Ansah A, Boadi-Kusi SB, *et al.* Occupational hazards correlates of ocular disorders in Ghanaian fisheries. *Healthc Low Resour Settings* 2016;**4**.
- 7. Guillén DE. Pterigión. Una guía práctica de diagnóstico y tratamiento. *Rev Med Hondur* 2005;**63:**99.
- 8. Dimitry TJ. The dust factor in the production of pterygium. *Am J Ophthalmol* 1937;**20:**40-5.
- 9. Dhir S, Detels R, Alexander E. The role of environmental factors in cataract, pterygium and trachoma. *Am J Ophthalmol* 1967;**64:**128-35.
- 10. Khoo J, Saw S-M, Banerjee K, *et al.* Outdoor work and the risk of pterygia: a case-control study. *Int Ophthalmol* 1998;**22:**293-8.
- 11. Saw SM, Banerjee K, Tan D. Risk factors for the development of pterygium in Singapore: A hospital based case control study. *Acta Ophthalmol* 2000;**78**:216-20.
- 12. BOOTH F. Heredity in one hundred patients admitted for excision of pterygia. *Clin Exp Ophthalmol* 1985;**13**:59-61.
- 13. Al Bdour MD, Al Latayfeh MtM. Risk factors for pterygium in an adult Jordanian population. Acta Ophthalmol 2004;82:64-7.
- 14. Starck T, Kenyon KR, Serrano F. Conjunctival autograft for primary and recurrent pterygia: surgical technique and problem management. *Cornea* 1991;**10**:196-202.
- 15. Taylor HR, West SK, Rosenthal FS, *et al.* Corneal changes associated with chronic UV irradiation. *Arch Ophthalmol* 1989;**107**:1481-4.
- 16. McCarty CA, Fu CL, Taylor HR. Epidemiology of pterygium in Victoria, Australia. *Br J Ophthalmol* 2000;**84:**289-92.
- 17. Saw S-M, Tan D. Pterygium: prevalence, demography and risk factors. *Ophthalmic Epidemiol* 1999;**6**:219-28.
- 18. Rezvan F, Khabazkhoob M, Hooshmand E, et al. Prevalence and risk factors of pterygium: a systematic review and meta-analysis. *Surv Ophthalmol* 2018.
- 19. Mackenzie FD, Hirst LW, Battistutta D, Green A. Risk analysis in the development of pterygia. *Ophthalmology* 1992;**99:**1056-61.
- 20. Dushku N, Reid TW. P53 expression in altered limbal basal cells of pingueculae, pterygia, and limbal tumors. *Curr Eye Res* 1997;**16:**1179-92.
- 21. Pérez Guerrero RM, Hornia Palacio M, Fernández Beatón M, Quiñones Rodríguez M. Pesquizaje oftalmológico en el área de salud. *Rev Cubana Oftalmol* 1989;**2:**103-9.
- 22. Arffa RC, Grayson M. Grayson's Diseases of the Cornea, Mosby Incorporated, 1997.
- 23. Aragonés Cruz B. Estudio prospectivo de trasplante conjuntival con células límbicas o sin ellas, en el pterigium primario. *Rev Cubana Oftalmol* 2006;**19:**0-.

- 24. Oyola J. El pterigion en el Hospital Cayetano Heredia y su prevalencia. *Rev Per Oftalmol* 1988;**14**:23-4.
- 25. Ukponmwan C, Dawoda O, Edema O, Okojie O. Prevalence of pterygium and pingueculum among motorcyclists in Nigeria. *East Afr Med J* 2007;**84:**516-21.
- 26. Rehm J, Room R, Graham K, *et al.* The relationship of average volume of alcohol consumption and patterns of drinking to burden of disease: an overview. *Addiction* 2003;**98**:1209-28.
- 27. Rehm J, Monteiro M. Alcohol consumption and burden of disease in the Americas: implications for alcohol policy. *Rev Panam Salud Publica* 2005;**18**:241-8.
- 28. Ng M, Freeman MK, Fleming TD, *et al.* Smoking prevalence and cigarette consumption in 187 countries, 1980-2012. *JAMA* 2014;**311**:183-92.
- 29. Marmamula S, Khanna RC, Rao GN. Population-based assessment of prevalence and risk factors for pterygium in the South Indian state of Andhra Pradesh: the Andhra Pradesh Eye Disease Study. *Invest Ophthalmol Vis Sci* 2013;**54:**5359-66.
- 30. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. *J Natl Cancer Inst* 1959;**22**:719-48.
- 31. Achigbu E, Ezepue U. Prevalence and severity of pterygium among commercial motorcycle riders in South Eastern Nigeria. *Ghana Med J* 2014;**48:**153-7.
- 32. Njinaka I, Uhumwangho OM, Edema OT, *et al.* A comparison study of conjunctiva disorders in technical and administrative sawmill workers in Nigeria. *Malays J Med Sci* 2011;**18**:43.
- 33. Lee KW, Choi Y-H, Hwang SH, *et al.* Outdoor Air Pollution and Pterygium in Korea. *J Korean Med Sci* 2017;**32:**143-50.