



Original article

Pterygium as a Manifestation of Chronic Ocular Microtrauma in Young Patients with Dry Eye Syndrome: Results of a Retrospective Multicenter Study

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Abstract

Objective: To establish morphological criteria for diagnosing clinical stages of pterygium using histological and immunohistochemical parameters and to evaluate pterygium as a possible manifestation of chronic ocular surface microtrauma associated with dry eye syndrome.

Methods. A retrospective, multicentre, non-interventional study was conducted. The clinical and epidemiological analysis covered the period from January 28, 2019, to December 25, 2024. The main clinical cohort included 219 patients who underwent surgical treatment for pterygium in 2022–2023. Age, sex, lesion localisation, clinical stage, disease duration, and recurrence were analysed. Excised pterygium tissues were examined histologically using hematoxylin and eosin staining. Epithelial dysplasia, stromal elastosis, vascular density, and inflammatory infiltration were assessed. Immunohistochemical analysis was performed using Ki-67 as a marker of proliferative activity and vascular endothelial growth factor as a marker of angiogenesis. Data were processed using descriptive statistics and cross-tabulation.

Results. The surgical conversion rate ranged from 0.53% in Astana to 6.67% in Semey. In one clinic in Astana, the number of pterygium surgeries increased by 284.2% in 2024 compared with 2019. Among 219 patients, men accounted for 51.6% and women for 48.4%. The mean patient age decreased by more than two years from 2022 to 2023. More than 94% of surgeries were performed at stages 2–3. Ki-67 expression increased from 2.1% at stage 1 to 55.8% at stage 4, while vascular endothelial growth factor expression increased from 10.5% to 92.7%.

Conclusions. Clinical progression of pterygium was associated with increasing histological severity and higher expression of Ki-67 and vascular endothelial growth factor. The findings support the interpretation of pterygium as an active pathological process involving chronic microtrauma, inflammation, angiogenesis, and abnormal wound healing rather than a purely degenerative lesion.

Keywords: pterygium, dry eye syndromes, immunohistochemistry, Ki-67 antigen, vascular endothelial growth factor A, angiogenesis, wound healing.

1. Introduction

Pterygium is a common chronic disease of the ocular surface, traditionally described as degenerative, but it can also be interpreted as a consequence of repeated microtrauma to the conjunctiva and corneal limbus. Tear film instability, dry eye syndrome, ultraviolet exposure, wind, dust, and blink-related friction may act as persistent damaging factors. Recurrent epithelial stress leads to inflammation, stromal remodelling, vascularisation, fibrosis, and gradual fibrovascular growth onto the cornea. The absence of unified morphological criteria for clinical staging makes diagnosis subjective and contributes to differences in therapeutic approaches. Therefore, clear morphological criteria are needed not only for staging, but also for assessing the severity of chronic tissue injury and choosing appropriate treatment tactics.

Clinical and morphological analysis has shown that the most informative histological signs of pterygium are elastosis, vascularisation, and subepithelial fibrosis. From a trauma perspective, these features reflect long-term ocular surface damage and repeated repair. They also help distinguish primary and recurrent pterygium and exclude similar lesions, including pyogenic granuloma. A. Gupta et al. [1] emphasised the importance of morphological verification for accurate clinical prognosis. The assessment of pterygium transparency also demonstrated reproducible results among clinicians with different levels of experience, suggesting that visual and morphological grading can be standardised. M. Hilmi [2] confirmed the possibility of reproducible morphological assessment even without automated systems.

A general review of pterygium aetiology and treatment also supports the need to supplement standard clinical diagnosis with structural assessment of the lesion. I. Ilmawati [3] confirmed the need to unify morphological classifications. This is especially relevant when pterygium is viewed not only as a degenerative lesion, but also as a chronic wound-healing response to repeated ocular surface injury. The connection between pterygium morphology and dry eye parameters is particularly important: invasion length, lesion height, and thickness correlate with tear osmolarity, tear production, and epithelial erosion. Early stages are often associated with desiccation changes, while progressive forms show stronger inflammation. D. Ha. and K. Kim [4] therefore demonstrated the value of morphometric parameters in assessing the patient's clinical condition.

Clinical and pathological comparisons show that vascular network severity and elastosis correlate with the macroscopic “fleshy” appearance of pterygium. These signs may indicate chronic irritation, microvascular activation, and stromal repair. Histological parameters also correspond to clinical lesion size. S. Lodhi et al. [5] noted that morphological features may help predict lesion aggressiveness. In an epidemiological analysis of more than 160 thousand patients, most pterygia were located along the nasal edge and were usually characterised by initial morphological stages. A. Das et al. [6] noted that not every lesion requires intervention, but morphological assessment remains important when planning surgery, especially in active or progressive cases.

Artificial intelligence may improve the early identification of pterygium morphotypes associated with chronic injury and progression. A deep learning model showed high accuracy in distinguishing clinically relevant stages and forms. W. Xu et al. [7] demonstrated the potential of automated systems to support morphological diagnosis. This is important for detecting lesions that may reflect active microtrauma, dry eye-related inflammation, or aggressive vascular growth. Studies of mitomycin-C use in different morphological types also showed that recurrence is more common in “fleshy” forms. F. Khan and S.P.K. Niazi [8] therefore stressed the importance of visual morphological assessment for predicting treatment outcomes.

The general prevalence of pterygium in Central Asian countries, including Kazakhstan, according to a population study by A. Hashemi et al. [9], is between 4% and 8% in the general adult population. In Kazakhstan, environmental factors such as wind, dust, ultraviolet exposure, and climate-related ocular surface dryness may contribute to chronic irritation. Therefore, early diagnosis of pterygium is especially important. Patient-oriented ophthalmic care requires standard clinical routes, trained personnel, and timely differentiation from other conjunctival conditions. Y. Rakhimova et al. [10] noted that insufficient differential diagnosis may delay referral of patients with advanced pterygium for morphological examination.

Automated diagnostic systems may also help detect early morphological signs before advanced fibrovascular invasion occurs. Intelligent expert systems based on ophthalmic image analysis may be adapted to recognise trauma-related changes in pterygium and support outpatient screening. O. Mamyrbayev et al. [11] highlighted the importance of

such technologies for pre-stratifying patients by lesion type.

The importance of early diagnosis is also supported by studies of other ophthalmic diseases. In age-related macular degeneration, timely and accurate diagnosis was shown to influence visual function and quality of life. Although this is a different disease, the same principle applies to pterygium: early detection of structural changes and inflammation may help prevent complications and reduce the need for late surgical intervention. I. Ismayilova et al. [12] demonstrated the relevance of a multidisciplinary approach, which is also applicable to pterygium when it is viewed as a chronic ocular surface injury involving clinical, morphological, inflammatory, and environmental factors.

Y. Nurlybekova et al. [13] analysed pathogenetic mechanisms of pterygium and focused on modern surgical techniques that reduce recurrence risk. They showed that an important surgical goal is to create a morphological barrier preventing fibrous tissue from

growing into the cornea. This supports the trauma-oriented model, because recurrent fibrous ingrowth can be interpreted as continuation of abnormal wound healing after chronic tissue injury. Their description of fibrous component formation is also relevant for developing morphological staging criteria.

Overall, the literature shows several gaps. First, there is still no unified morphological classification of pterygium stages, which makes comparison between studies difficult. Second, clinical and instrumental findings are not always sufficiently integrated with morphological verification. Third, few studies in Kazakhstan have examined pterygium through the combined perspective of clinical morphology, chronic ocular surface damage, and biological activity. Therefore, the present study aimed to establish morphological criteria for diagnosing clinical stages of pterygium using histological and immunohistochemical parameters.

2. Materials and Methods

Research design and ethical aspects

A retrospective, multicentre, non-interventional study was conducted using clinical, epidemiological, and pathomorphological data. The clinical and epidemiological phase covered the period from January 28, 2019, to December 25, 2024, and the in-depth clinical cohort analysis and pathomorphological study covered the period from January 1, 2022, to December 31, 2023.

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Permission to conduct the study was obtained from the Ethics Committee of the Multidisciplinary City Hospital No. 3 in Astana before data collection. The study was based on retrospective analysis of depersonalised medical records and archived surgical material. All data were anonymised before analysis, and no information allowing patient identification was used in the manuscript. Given the retrospective and anonymised nature of the study, the requirement for individual written informed consent was waived by the Ethics Committee.

Data sources and sample formation

Data were obtained from three main sources. First, generalised statistical data from the Astana Vision network of ophthalmic clinics were used to assess regional differences in diagnosis and surgical treatment. The analysed branches included Pavlodar, Shymkent, Semey, Ust-Kamenogorsk, Astana, Almaty, and Karaganda. Second, surgical statistics from the Astramed clinic in Astana were used to evaluate the dynamics of pterygium operations over time. Third, the main clinical cohort was formed from patients treated

surgically at the Multidisciplinary City Hospital No. 3 of the Astana Akimat.

The clinical cohort included all patients who met the inclusion criteria and underwent surgery during 2022-2023. Inclusion criteria were a confirmed diagnosis of pterygium, surgical treatment in hospital conditions, and complete medical documentation containing demographic and clinical data. Exclusion criteria were incomplete records or concomitant conjunctival pathology that could affect interpretation, such as pseudopterygium or conjunctival intraepithelial neoplasia. A total of 219 patients were included, comprising 134 patients in 2022 and 85 patients in 2023.

Clinical variables and trauma-oriented interpretation

Clinical and demographic information was collected by analysing and systematising data from the medical records of inpatients. The following indicators were recorded: age, gender, location of the lesion (right eye – OD, left eye – OS, both eyes – OU), clinical stage of pterygium, anamnestic duration of the disease, and the presence of relapse. Clinical staging was performed by attending ophthalmologists based on a standard biomicroscopic examination.

Patients aged 20-39 and 40-49 were reviewed as groups in which pterygium may be less dependent on ageing and more related to chronic ocular surface stress, tear film instability, occupational exposure, environmental irritation or repeated mechanical friction

Statistical analysis

Statistical analysis of the obtained data was performed using Microsoft Excel 2019 software. Descriptive statistical methods were used. Mean values,

standard deviations, medians, ranges, frequencies, and percentages were calculated.

To compare regional surgical activity, a surgical conversion rate (SCR) was calculated using the formula:

$$SCR = (NO / ND) \times 100\%, \quad (1)$$

where NO – average number of operations; ND – average number of diagnoses. Cross-tabulation methods were used to explore the relationships between different parameters (for example, age and stage, gender and stage).

Pathomorphological and immunohistochemical studies

Removed pterygium tissue was fixed in 10% neutral buffered formalin for 24 hours, processed according to standard histological protocols, embedded

in paraffin, sectioned at 4-5 microns, and stained with hematoxylin and eosin. A pathomorphologist assessed epithelial dysplasia, stromal elastosis, vascular density, and inflammatory infiltration using a semi-quantitative approach.

Immunohistochemical analysis was performed on paraffin sections using monoclonal antibodies to Ki-67 and VEGF. Ki-67 was selected as a marker of epithelial proliferative activity, while VEGF was selected as a marker of angiogenesis. The reaction was visualised using a polymer detection system with DAB chromogen. Marker expression was quantified as the percentage of positively stained cells in 10 representative high-power fields at ×400 magnification using ImageJ software.

3. Results

Regional surgical activity and epidemiological context

The surgical conversion rate was used to reduce the influence of differences in total patient flow

between clinics. This rate was calculated according to Formula 1 based on average data for the period 2022-2024 (Table 1).

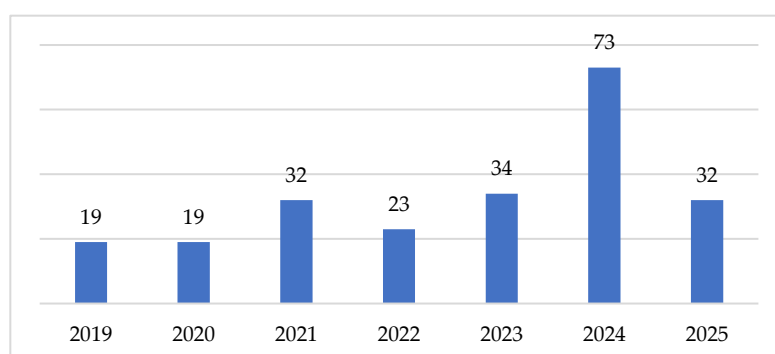


Figure 1 - Dynamics of the number of operations to remove pterygium in the Astramed clinic (Astana) for 2019-2025

The SCR varied substantially between regions. Semey had the highest rate at 6.67%, meaning that approximately seven out of every 100 diagnosed

patients underwent surgery. Ust-Kamenogorsk and Shymkent also showed relatively high rates, at 3.28% and 2.65%.

Table 1 - SCR for pterygium in the regions of Kazakhstan according to the network of clinics "Astana vision" (average data for 2022-2024)

City	Average number of diagnostics (n)	Average number of operations (n)	SCR (%)
Pavlodar	4475	65	1.45
Shymkent	8836	234	2.65
Families	4005	267	6.67
Ust-Kamenogorsk	7196	236	3.28
Astana	23375	124	0.53
Almaty	11977	79	0.66
Karaganda	6914	85	1.23

Note: SCR calculated as the ratio of the average number of operations to the average number of diagnoses, expressed as a percentage

In contrast, Astana and Almaty had the lowest rates, at 0.53% and 0.66%. The SCR in Semey was more than 12 times higher than in Astana. Pavlodar and Karaganda occupied intermediate positions.

Clinical cohort and demographic structure

The main clinical cohort included 219 patients who underwent surgical treatment for pterygium in 2022–2023. Of these, 134 patients were treated in 2022 and 85 patients in 2023. The distribution by sex is presented in Table 2.

Table 2 - Distribution of patients by gender for the period 2022-2023

Year	Number of men (n)	% of the total amount for the year	Number of women (n)	% of the total amount for the year	Total patients (n)
2022	63	47.0	71	53.0	134
2023	50	58.8	35	41.2	85
Total	113	51.6	106	48.4	219

During the two-year period, men accounted for 51.6% of patients and women for 48.4%. In 2022, women predominated, accounting for 53.0% of patients. In 2023, men predominated, accounting for 58.8% of patients.

The descriptive age statistics are presented in Table 3. The mean age of men decreased from 58.1 years in 2022 to 55.9 years in 2023.

Table 3 - Descriptive statistics of the age of patients (in years) who underwent surgery for pterygium

Indicator	Men 2022 (n=63)	Women 2022 (n=71)	Men 2023 (n=50)	Women 2023 (n=35)
Average age	58.1	59.4	55.9	57.2
Median	60.0	61.0	58.5	59.0
Age range	29-82	32-82	28-86	34-83

The mean age of women decreased from 59.4 years in 2022 to 57.2 years in 2023. The age range was 28–86 years.

The age and sex distribution is presented in Table 4. The largest group consisted of patients aged 60 years and older. Patients younger than 40 years were also represented in both years of observation.

Table 4 - Age-gender distribution of patients with pterygium in 2022 and 2023

Age group (years)	Men 2022 (n)	Women 2022 (n)	Men 2023 (n)	Women 2023 (n)
20-29	1	0	1	0
30-39	4	6	4	5
40-49	10	8	11	3
50-59	16	15	7	3
60 and older	32	42	27	24
Total	63	71	50	35

Disease duration, localisation, and bilateral involvement

Data on disease duration were limited, but one clinically important case involved a patient with a severe progressive pterygium between stages 3 and 4 and a recorded disease duration of four years. This suggests that advanced pterygium may result from prolonged untreated or insufficiently controlled ocular

surface injury. A chronic trauma model is consistent with this observation; persistent tear film instability and repeated epithelial damage may gradually transform a small lesion into a biologically active fibrovascular growth. The distribution of patients by localisation of the pathological process in the context of gender and year of follow-up is presented in Table 5.

Table 5 - Distribution of patients by lesion location, gender, and year

Localisation	Men		Women	
	2022 (n=63)	2023 (n=50)	2022 (n=71)	2023 (n=35)
OD (right eye)	23	20	34	14
OS (left eye)	38	27	30	16
OU (both eyes)	2	3	7	5

Men showed persistent predominance of left-eye lesions in both years. Women showed a predominance of right-eye lesions in 2022 but shifted toward left-eye predominance in 2023 (Table 6). Bilateral pterygium was less common but more frequent in women than

men. The proportion of bilateral involvement in women increased from 9.9% in 2022 to 14.3% in 2023.

Bilateral pterygium was usually asymmetric. In 2022, all bilateral cases showed different stages between eyes. In 2023, asymmetry remained dominant, although some symmetric cases were observed.

Table 6 - Characteristics of lesion asymmetry in bilateral pterygium (OU)

Year	Number of OU cases (n)	With symmetric stage (n)	With an asymmetric stage (n)	Prevalence of right eye damage (OD>OS) (n)	Predominance of left eye damage (OS>OD) (n)
2022	9	0	9	2	7
2023	8	3	5	2	3

The predominance of one eye in bilateral disease suggests that local exposure, mechanical factors, ocular surface microenvironment, eyelid dynamics, or asymmetric tear film instability may influence progression.

Clinical stage distribution

Clinical stage at the time of hospitalisation reflects when patients usually reach surgical treatment. The distribution is shown in Table 7.

Table 7 - Distribution of patients by clinical stage of pterygium, gender, and year

Clinical stage	Men		Women	
	2022 (n=63)	2023 (n=50)	2022 (n=71)	2023 (n=35)
Stage 1	0	2	1	4
Stage 2	55	38	58	26
Stage 3	8	8	10	5
Stage 4	0	1	2	0

Note: in cases of bilateral damage, a higher stage was considered

Most patients underwent surgery at stage 2. Stage 3 was the second most common. Extreme stages were rare: stage 1 operations were isolated, and stage 4 was uncommon. Overall, more than 94% of patients were treated surgically at stages 2-3. This suggests that pterygium usually becomes surgically relevant after it has progressed beyond early ocular surface changes.

From a trauma-oriented perspective, this is important. If pterygium develops through repeated microtrauma and chronic repair, then the optimal preventive window may be before the lesion reaches stage 2. Early identification of dry eye syndrome, tear film instability, and limbal irritation may reduce progression or delay surgery.

Table 8 - Distribution of patients by clinical stages in different age groups (total data for 2022-2023)

Age group (years)	Stage 1 (n)	Stage 2 (n)	Stage 3 (n)	Stage 4 (n)	Total (n)
20-39	2	18	1	0	21
40-59	5	76	15	2	98
60 and older	0	93	30	2	125
Total	7	187	46	4	244

Note: the total number (244) exceeds the number of patients (219) due to the fact that in cases of bilateral asymmetric lesions, both eyes with different stages were considered

The proportion of advanced stages increased with age. Stages 3-4 were rare in patients aged 20-39 but increased in patients aged 40-59 and were most frequent in those aged 60 and older (Table 8). This confirms that cumulative exposure and duration remain important. However, the presence of stage 2 disease in young patients indicates that clinically meaningful fibrovascular growth can occur early,

possibly when chronic ocular surface trauma is intense or persistent.

A comparative analysis of the distribution by stage among men and women within the same age group was performed to explore in more depth the possible effect of gender on the clinical course of pterygium (Table 9). The largest group of middle-aged patients (40-59 years) was selected for the analysis.

Table 9 - Comparative distribution by clinical stages among men and women in the age group 40-59 years (total data for 2022-2023)

Clinical stage	Men 40-59 years old (n=52)	Women aged 40-59 (n=46)
Stage 1	1	4
Stage 2	40	36
Stage 3	10	5
Stage 4	1	1

In the 40-59 group, men had a higher proportion of stages 3-4, while women were more frequently represented at stage 1. This may suggest later presentation or greater exposure among men, although behavioural and occupational factors require further study.

Recurrence and metachronous involvement

In 2023, two cases were documented as recurrent pterygium, representing 2.35% of patients that year. Both occurred in patients aged 50-59. In addition, comparison of 2022 and 2023 records identified at least three patients who underwent surgery on one eye in 2022 and required surgery on the paired eye in 2023. These cases were not classical same-eye recurrences but metachronous bilateral disease.

This pattern supports the idea that some patients have a systemic or bilateral ocular surface predisposition. Dry eye syndrome, environmental exposure, inflammatory susceptibility, or tear film instability may affect both eyes, even if clinical progression is asymmetric. Such patients may require long-term bilateral monitoring after the first operation.

Pathomorphological characteristics of clinical stages of pterygium

Histological examination demonstrated consistent structural progression across clinical stages. The main parameters were epithelial dysplasia, stromal elastosis, vascular density, and inflammatory infiltrate. The systematised histological characteristics of pterygium tissues corresponding to different clinical stages are presented in Table 10.

Table 10 - Histological characteristics of pterygium tissues at various clinical stages

Clinical stage	Characteristics of the epithelium (degree of dysplasia)	Stroma characteristics (degree of elastosis)	Vascular component (density)	Inflammatory infiltrate (intensity)
Stage 1	None	Insignificant	Low	Minimum
Stage 2	Mild atypia	Moderate	Moderate	Moderate
Stage 3	Moderate dysplasia	Expressed	High	Expressed
Stage 4	Severe dysplasia / CIS	Pronounced	Excessive	Intensive

The histological pattern changed from mild stromal degeneration and minimal inflammation in early stages to marked epithelial atypia, pronounced elastosis, high vascular density, and intense inflammatory infiltration in advanced stages. Stage 4

showed severe dysplasia or carcinoma in situ, emphasising the need for oncological vigilance in advanced or atypical lesions.

These findings are compatible with the chronic trauma model. Repeated microinjury of the ocular

surface may first produce epithelial stress and inflammatory activation. Over time, persistent repair may lead to stromal remodelling, fibrovascular proliferation, and dysplastic epithelial changes. In this model, dry eye syndrome functions as a mechanical and inflammatory amplifier.

Immunohistochemical expression of Ki-67 and VEGF

Immunohistochemistry was performed to quantify biological activity. Ki-67 reflected epithelial

proliferation, while VEGF reflected angiogenesis. The results of the quantitative assessment of the expression of proliferation and angiogenesis markers are presented in Table 11.

Both markers increased strongly with clinical stage. Ki-67 increased more than 25-fold from stage 1 to stage 4, demonstrating a major rise in epithelial proliferative activity. VEGF increased almost nine-fold, confirming progressive angiogenic activation.

Table 11 - Indicators of expression of Ki-67 and VEGF markers at various clinical stages of pterygium

Clinical stage	Ki-67 proliferation index (%) (mean ±SD)	VEGF expression (%) (mean ±SD)
Stage 1	2.1±0.8	10.5±2.8
Stage 2	8.5±2.3	35.2±5.1
Stage 3	25.3±4.1	68.9±7.3
Stage 4	55.8±6.7	92.7±6.8

These results provide objective support for the view that pterygium is biologically active, especially in advanced stages. In the context of chronic microtrauma, persistent epithelial injury and inflammation may

stimulate proliferation and angiogenesis as part of wound repair. When this response becomes chronic, it may lead to pathological fibrovascular growth.

4. Discussion

This study supports a stage-dependent model of pterygium progression in which clinical severity corresponds to increasing histological and immunohistochemical activity. The strongest evidence is the progressive rise in Ki-67 and VEGF expression from stage 1 to stage 4. These markers indicate that pterygium is not simply a static degenerative membrane but an active lesion characterised by epithelial proliferation, angiogenesis, inflammation, and stromal remodelling. Classical explanations of pterygium emphasise ultraviolet radiation, dust, wind, and age-related degeneration. These factors remain important, especially in older patients and outdoor workers. However, when pterygium appears or progresses in younger adults, the role of chronic ocular surface microtrauma should be considered more actively. Dry eye syndrome is one of the most plausible mechanisms linking environmental exposure, mechanical friction, inflammation, and abnormal wound healing.

The regional differences in surgical conversion rate may reflect variation in referral pathways, surgical availability, environmental exposure, patient awareness, clinician preference, or disease stage at presentation. The increase in surgical activity in Astana may be associated with improved access to surgery, greater recognition of progressive pterygium, or an increasing number of patients requiring surgical treatment after unsuccessful conservative management.

However, these assumptions require further prospective confirmation.

The presence of surgically treated pterygium in younger and middle-aged patients supports the need to consider not only cumulative ultraviolet exposure and age-related degeneration, but also chronic ocular surface microtrauma, dry eye syndrome, occupational exposure, environmental irritation, and tear film instability. In this model, an unstable tear film may increase blink-related friction and epithelial stress, contributing to inflammation, angiogenesis, fibrovascular proliferation, and abnormal wound healing.

A normal tear film protects the ocular surface from friction. When the tear film becomes unstable, the eyelid repeatedly rubs against a vulnerable epithelium. Blinking, which is normally protective, becomes a source of microtrauma. This repeated injury is particularly important at the limbus, where epithelial regeneration, vascular signalling, and inflammatory responses are active. Over time, dry eye-related friction may contribute to epithelial damage, inflammatory mediator release, fibroblast activation, and new vessel formation.

The histological findings in this study align with that model. Early lesions had minimal inflammation and low vascularity, while advanced lesions showed stronger inflammatory infiltration, vascular density, stromal elastosis, and epithelial dysplasia. This

sequence resembles chronic wound repair: injury is followed by inflammation, matrix remodelling, angiogenesis, and epithelial proliferation. The problem is that in pterygium this repair response becomes persistent and anatomically disorganised.

In the study by S. Ghosh et al. [14], the expression of VEGF and Ki-67 in samples of pterygium and adjacent healthy conjunctiva was analysed. The results showed no statistically significant differences between the groups. The authors suggested that the pathological process may cover the entire surface of the eye, including “normal” tissue. This contradicts the results of the study, where healthy tissues did not show increased expression. The likely cause of discrepancies may be the location of the control tissue (from the same eye, next to the pathology), which may have given a blurred molecular profile.

Analysis of VEGF expression confirmed that angiogenesis is a key mechanism in pterygium pathogenesis, especially in advanced stages, where VEGF increased almost ninefold compared with the initial stage. This was supported by both histological and immunohistochemical findings. J. Martín-López et al. [15] showed that VEGF-165, one of the VEGF-A isoforms, contributes to a shift toward angiogenesis rather than lymphangiogenesis, with an increased blood-to-lymphatic vessel ratio. These findings are partially consistent with the present study, although their work focused on a specific VEGF isoform and microvascular remodelling, while the current study assessed total VEGF expression.

Immunohistochemistry also showed a marked increase in VEGF expression in stages III-IV, suggesting that angiogenesis may be a potential therapeutic target, including through VEGF inhibition. M. Turan et al. [16] similarly reported high VEGF expression in recurrent pterygium and additionally highlighted the role of inflammation through Cyclophilin A. Their findings complement the present study, although they focus on recurrence rather than stage-dependent progression.

The age and gender analysis showed a decrease in the average age of surgically treated patients by more than two years in 2023 compared with 2022. The proportion of men aged 40-49 years and women aged 30-39 years also increased, which may indicate earlier presentation or a higher frequency of active forms in younger groups. M. Turan and G. Turan [17] did not focus on age dynamics, but they reported increased Ki-67 and Bcl-2 expression regardless of age, including in younger patients, which partially supports the present findings.

The study revealed regional differences in surgical conversion rate, an increase in operations in Astana, a trend toward disease “rejuvenation,” and a correlation

between clinical stage and microscopic severity, especially Ki-67 and VEGF expression. C. Masitas et al. [18] showed that MMP-14 plays a role in fibrosis and recurrence of pterygium, suggesting that targeted treatment may be useful at specific morphological stages. Unlike their molecular focus, the present study emphasised quantitative histological and immunohistochemical indicators of severity and progression.

S. Bergeron et al. [19] reported significant histopathological variability in pterygium and noted that clinical stage does not always directly correspond to histological severity. This contrasts with the present study, where morphological criteria showed a clearer relationship with clinical stage. The difference may be explained by variations in study populations, classification methods, and inclusion of concomitant lesions.

A.C.V. Wanzeler et al. [20] reviewed multiple molecular mechanisms involved in pterygium development, including gene methylation, inflammatory mediators, microsatellite instability, and cholesterol metabolism. These findings show that pterygium pathogenesis is complex and cannot be fully explained by morphology alone. Therefore, molecular approaches may complement classical histological staging and improve personalised prognosis.

The present study used traditional clinical and morphological methods, while Q. Ji et al. [21] proposed an automated grading system based on deep learning and semantic segmentation of anterior eye images. Their model showed high agreement with clinicians and allowed non-invasive quantification of lesion size and invasion. This suggests that artificial intelligence may improve objectivity and support future integration with classical morphology.

E.W.W. Tiong et al. [22] also demonstrated high diagnostic accuracy of deep learning systems using nearly 46,000 images, with sensitivity of 98.1% and specificity of 99.1%. However, they noted limitations related to selection bias and lack of external validation. These findings contrast with the present study’s histological and immunohistochemical approach, but they highlight the potential of non-invasive digital screening.

D. Ghorab et al. [23] showed that a broader immunohistochemical panel, including glutathione, topoisomerase 1, p53, and VEGF, may help distinguish primary and recurrent pterygium. This suggests that Ki-67 and VEGF, although useful, may not be sufficient alone for universal prediction. A wider biomarker panel may be needed for more accurate risk stratification.

The present study analysed epidemiology, morphology, immunohistochemistry, and surgical

dynamics in Kazakhstan. M. Palewski et al. [24] reviewed surgical methods and showed that recurrence rates vary widely, from 6.7% to 88%, depending on technique. This indicates that surgical standardisation is also crucial and may influence outcomes independently of regional differences.

B. Chen et al. [25] discussed artificial intelligence in pterygium diagnosis and showed that modern AI systems can classify and localise pterygium with accuracy comparable to experienced clinicians. M. Khan et al. [26] compared surgical techniques and found that recurrence was more related to stromal features than epithelial characteristics. These findings differ from the present study, which focused on clinical stage, epithelial proliferation, and angiogenesis.

Recent studies also expand the understanding of pterygium pathogenesis. J. Yang et al. [27] identified FN1, SPRR1B, SERPINB13, and EGR2 as potential biomarkers and showed increased Th2 lymphocyte infiltration, highlighting the role of the immune microenvironment. H. Ge et al. [28] described a minimally invasive surgical protocol without scalpel or electrocoagulation, associated with low pain and a recurrence rate of 4.3%. J. Wolf et al. [29] used sequencing and immunohistochemistry to identify fibrosis, autophagy, and apoptosis modulation as important disease mechanisms. These findings support a broader, multifactorial view of pterygium.

The present study included 219 patients in Kazakhstan and found that men accounted for 51.6% and women for 48.4% of cases. The average age decreased from 58.1-59.4 years in 2022 to 55.9-57.2 years in 2023. Most patients underwent surgery at stage 2, while Ki-67 increased from 2.1% at stage 1 to 55.8% at stage 4, and VEGF increased from 10.5% to 92.7%. The surgical conversion rate ranged from 0.53% in Astana to 6.67% in Semey, and the number of operations increased by 284.2% in 2024 compared with 2019.

J. Yu et al. [30] identified 536 differentially expressed genes and 78 circRNAs involved in IL-17,

extracellular matrix receptor interaction, and epithelial-mesenchymal transition pathways. These molecular findings partially overlap with the present study's focus on proliferation and angiogenesis but provide a deeper regulatory explanation. S.A. Gujrathi et al. [31] reported male predominance, a dominant 50-60-year age group, and mostly nasal lesions, which differs from the more balanced gender structure in the Kazakh cohort. Y. Xu et al. [32] described the LINC00472-miRNA-mRNA regulatory network, including pathways related to pterygium progression, supporting the role of genetic regulation in proliferation and angiogenesis.

Thus, the correlation between clinical stage and Ki-67 and VEGF expression supports the use of morphological and immunohistochemical criteria for objective pterygium staging. At the same time, regional differences, younger patient presentation, artificial intelligence, and molecular studies indicate the need to combine classical morphology with modern diagnostic and personalised treatment approaches.

Strengths and limitations

The strengths of this study include the combined clinical, epidemiological, histological, and immunohistochemical assessment of pterygium, the inclusion of 219 surgically treated patients, and the analysis of regional surgical activity in Kazakhstan. The use of Ki-67 and vascular endothelial growth factor allowed the biological activity of pterygium to be assessed across clinical stages. However, the study also has limitations. Its retrospective design limits causal interpretation. Data on disease duration and dry eye parameters were incomplete. Tear film stability, ocular surface staining, tear osmolarity, and symptom severity were not systematically assessed. The study did not include a prospective control group, and the statistical analysis was mainly descriptive. Future prospective studies should directly evaluate dry eye syndrome parameters and correlate them with clinical stage, lesion morphology, recurrence, and immunohistochemical activity.

5. Conclusions

This study analysed pterygium in Kazakhstan using clinical, epidemiological, histological, and immunohistochemical data and showed that clinical progression of the disease was associated with increasing morphological severity and higher biological activity. The surgical conversion rate varied from 0.53% in Astana to 6.67% in Semey, while surgical activity in one Astana clinic increased by 284.2% between 2019 and 2024. Among 219 surgically treated patients, men accounted for 51.6% and women for 48.4%, and the mean age decreased by more than two years from 2022 to 2023. Most operations were performed at stages 2-3.

Histological examination showed progressive epithelial dysplasia, stromal elastosis, vascularisation, and inflammatory infiltration, while immunohistochemistry demonstrated an increase in Ki-67 expression from 2.1% to 55.8% and vascular endothelial growth factor expression from 10.5% to 92.7% from stage 1 to stage 4. These findings support the interpretation of pterygium as an active pathological process involving chronic ocular surface microtrauma, inflammation, angiogenesis, and abnormal wound healing, especially in patients with factors associated with dry eye syndrome. Future

prospective studies should directly assess dry eye parameters and correlate them with clinical stage, lesion progression, recurrence, and surgical outcomes.

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AI Declaration. During the preparation of this work the authors used (Grammarly) in order to improve the English language, grammar, and readability. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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Птеригиум құрғақ көз синдромы бар жас науқастардағы көз беткейінің созылмалы микрожарақаттануының көрінісі ретінде: Ретроспективті көпорталықты зерттеу нәтижелері

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Түйіндеме

Зерттеудің мақсаты: птеригиумның клиникалық сатыларын диагностикалауға арналған морфологиялық критерийлерді гистологиялық және иммуногистохимиялық көрсеткіштер негізінде анықтау, сондай-ақ птеригиумды құрғақ көз синдромымен байланысты көз беткейінің созылмалы микрожарақаттануының ықтимал көрінісі ретінде бағалау.

Әдістері. Ретроспективті, көпорталықты, интервенциялық емес зерттеу жүргізілді. Клиникалық-эпидемиологиялық талдау 2019 жылғы 28 қаңтардан 2024 жылғы 25 желтоқсанға дейінгі кезеңді қамтыды. Негізгі клиникалық когортаға 2022–2023 жылдары птеригиум бойынша хирургиялық ем алған 219 науқас енгізілді. Жасы, жынысы, зақымдану жағы, клиникалық сатысы, ауру ұзақтығы және қайталану жағдайлары талданды. Алынған тіндер гематоксилин және эозинмен бояу арқылы гистологиялық жолмен зерттелді. Эпителиалды дисплазия, стромалық эластоз, тамырлық тығыздық және қабыну инфильтрациясы бағаланды. Иммуногистохимиялық зерттеу Ki-67 пролиферативтік белсенділік маркері және тамырлық эндотелиалдық өсу факторы ангиогенез маркері ретінде қолданылып жүргізілді. Деректер сипаттамалық статистика және айқас кестелер әдістерімен өңделді.

Нәтижелері. Хирургиялық конверсия көрсеткіші Астанада 0,53%-дан Семейде 6,67%-ға дейін өзгерді. Астанадағы бір клиникада птеригиум бойынша ота саны 2024 жылы 2019 жылмен салыстырғанда 284,2%-ға артты. 219 науқастың 51,6%-ы ерлер, 48,4%-ы әйелдер болды. Науқастардың орташа жасы 2022 жылдан 2023 жылға қарай екі жылдан астам төмендеді. Оталардың 94%-дан астамы 2–3-сатыларда жасалды. Ki-67 экспрессиясы 1-сатыда 2,1%-дан 4-сатыда 55,8%-ға дейін, ал тамырлық эндотелиалдық өсу факторының экспрессиясы 10,5%-дан 92,7%-ға дейін артты.

Қорытынды. Птеригиумның клиникалық үдеуі гистологиялық өзгерістердің айқындылығының артуымен және Ki-67 мен тамырлық эндотелиалдық өсу факторы экспрессиясының жоғарылауымен байланысты болды. Алынған деректер птеригиумды тек дегенеративті зақымдану ретінде емес, созылмалы микрожарақаттану, қабыну, ангиогенез және тіндердің патологиялық жазылу үдерістерімен байланысты белсенді патологиялық процесс ретінде қарастыруға мүмкіндік береді.

Түйін сөздер: птеригиум, құрғақ көз синдромы, иммуногистохимия, Ki-67 антигені, тамырлық эндотелиалдық өсу факторы А, ангиогенез, жараның жазылуы.

Птеригиум как проявление хронической микротравматизации глазной поверхности у молодых пациентов с синдромом сухого глаза: Результаты ретроспективного многоцентрового исследования

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Резюме

Цель исследования: определить морфологические критерии диагностики клинических стадий птеригиума на основании гистологических и иммуногистохимических показателей, а также оценить птеригиум как возможное проявление хронической микротравматизации глазной поверхности, ассоциированной с синдромом сухого глаза.

Методы. Проведено ретроспективное многоцентровое неинтервенционное исследование. Клинико-эпидемиологический этап охватывал период с 28 января 2019 года по 25 декабря 2024 года. Основная клиническая когорта включала 219 пациентов, прооперированных по поводу птеригиума в 2022–2023 годах. Анализировались возраст, пол, локализация поражения, клиническая стадия, длительность заболевания и наличие рецидива. Удаленные ткани исследовались гистологически с окраской гематоксилином и эозином. Оценивались эпителиальная дисплазия, стромальный эластоз, сосудистая плотность и воспалительная инфильтрация. Иммуногистохимическое исследование проводилось с использованием Ki-67 как маркера пролиферативной активности и сосудистого эндотелиального фактора роста как маркера ангиогенеза. Данные обрабатывались методами описательной статистики и перекрестных таблиц.

Результаты. Показатель хирургической конверсии варьировал от 0,53% в Астане до 6,67% в Семее. В одной клинике Астаны количество операций по поводу птеригиума увеличилось на 284,2% в 2024 году по сравнению с 2019 годом. Среди 219 пациентов мужчины составили 51,6%, женщины — 48,4%. Средний возраст пациентов снизился более чем на два года с 2022 по 2023 год. Более 94% операций выполнялись на 2–3 стадиях. Экспрессия Ki-67 увеличилась с 2,1% при 1 стадии до 55,8% при 4 стадии, а экспрессия сосудистого эндотелиального фактора роста — с 10,5% до 92,7%.

Выводы. Клиническое прогрессирование птеригиума было связано с нарастанием гистологической выраженности изменений и повышением экспрессии Ki-67 и сосудистого эндотелиального фактора роста. Полученные данные позволяют рассматривать птеригиум как активный патологический процесс, включающий хроническую микротравматизацию, воспаление, ангиогенез и нарушение процессов заживления тканей, а не только как дегенеративное поражение.

Ключевые слова: птеригиум, синдром сухого глаза, иммуногистохимия, антиген Ki-67, сосудистый эндотелиальный фактор роста А, ангиогенез, заживление ран.