

# A Prospective Study Evaluating Correlation Between Preoperative Histopathology And Morphology with Recurrence Of Pterygium After CLAU Surgery

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## Abstract

**Aim-** To observe recurrence rate after conjunctival limbal autograft (CLAU) and to correlate this with preoperative histopathological and morphological characteristics of pterygium.

**Design:** Interventional, Prospective, Hospital-Based Study.

**Methods:** 107 patients with primary pterygium were examined, managed by CLAU and histopathology sample sent. The outcomes were assessed in terms of clinically significant or insignificant recurrence till 6 months follow-up.

**Results:** 57% patients were female. 17.8% participants had Stockers Line and all patients having stocker's line had stationary type of pterygium. Fuchs spots were seen in 4.7% of patients. Histopathology findings include Epithelial Hyperplasia (80.4%), Vascularity Overwhelms Fibrosis (39.1%), Vascularity Similar to Fibrosis (28.3%), Fibrosis Overwhelms Vascularity (34.8%), Perivascular Stromal Inflammation (54.3%), Diffuse Stromal Inflammation (37.0%). The following variables were significantly associated ( $p < 0.05$ ) with the Recurrence: Age, Fuchs Spots, higher vascularity and Diffuse Stromal Inflammation on histopathology.

**Conclusion:** Factors such as younger age group, higher redness and thickness of pterygium, Fuchs Spots, higher vascularity and diffuse inflammation on histopathological examination can be considered as a risk factor for recurrence. However, occupation, laterality, location and type of pterygium were found not to be related to recurrence.

**Keywords:** Recurrence, Pterygium, Conjunctival limbal autograft, Histopathology.

## 1. INTRODUCTION

Pterygium has been titled as an ophthalmic enigma, as much is still under disguise about this disease, despite being a much prevalent condition.<sup>[1]</sup> Clinically, pterygium has been defined as a wing-shaped fibrovascular lesion in the palpebral fissure extending from the bulbar conjunctiva onto the cornea. In this condition, conjunctiva undergoes elastotic degeneration and proliferation as a granulation tissue that is eventually vascularized to invade the cornea, damaging the superficial layers of stroma and Bowman's membrane. Underlying mechanism is considered to be a result of altered epithelial cell proliferation and vascularization.<sup>[2],[3]</sup> However, the precise pathogenesis is still under question.

Histopathological features of pterygium are characterized by the presence of a combination of elastotic degeneration of collagen with fibrovascular proliferation, and vascular density,

leukocytic infiltration, subepithelial and stromal fibrosis.<sup>[4],[5],[6]</sup> Its definitive management is surgical excision. Different surgeries have been developed throughout different ages to attain minimal recurrence and astigmatism with ocular surface rehabilitation, and excellent cosmesis. The most common complication encountered after pterygium excision is recurrence.<sup>[7]</sup>

Conjunctival limbal autograft (CLAU) was found to be more efficient than other surgeries to preclude pterygium recurrence after a 6-month follow-up, especially in recurrent pterygia.<sup>[8]</sup> Post operative inflammation has been thought to be a main cause behind recurrence and in CLAU surgery limbal cell transplantation following excision has an anti-inflammatory and anti-angiogenic effect, and thus lowers recurrence rates.<sup>[9]</sup> However, the precise mechanism is still under question.

Previous studies highlighted features such as grade, laterality, size of pterygium and histopathological parameters like inflammation, vascularity and fibrosis might have some correlation with recurrence.

Since recurrence is considered a significant hurdle in the success of pterygium surgeries, therefore this study was conducted to assess the recurrence rate of pterygium after CLAU, the role of morphological and histopathological features in its development.

## 2. MATERIAL AND METHOD

This study was carried out in 107 eyes of 107 patients having pterygium, attending eye OPD at M.Y. Hospital and M.G.M Medical College, Indore, M.P. from duration 01 Year 2019 to 2020. Informed consent was taken from patients before enrolling them for study. Approval from institutional ethical committee was taken. Patients having age group of 20-70 years with pterygium undergoing surgery for decreased visual acuity and/or cosmetic reasons were included in this study. Exclusion criteria were patients having pseudopterygium and/or coexisting conjunctival diseases and patients with fibrovascular proliferation of conjunctiva.

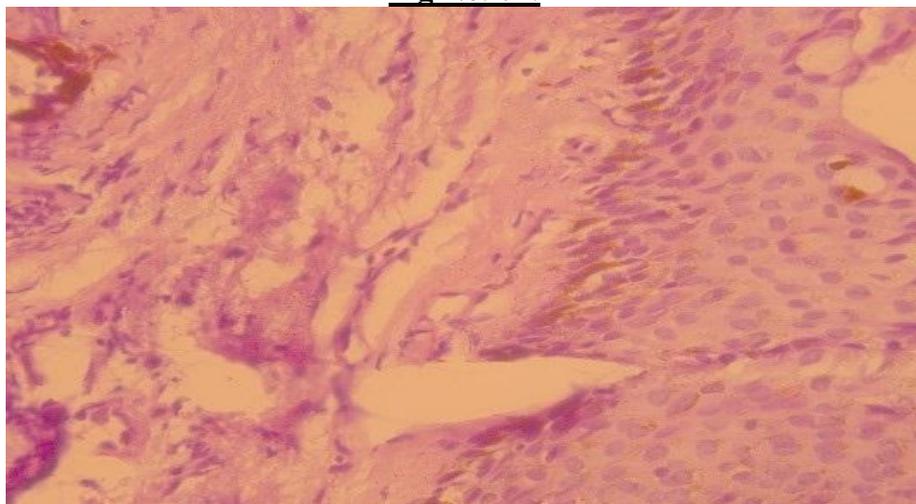
These patients were examined thoroughly on slit-lamp biomicroscope and clinical parameters were noted such as site of pterygium (nasal/temporal), laterality (unilateral/bilateral), type of pterygium (stationary/progressive/regressive), presence of Stocker's line (defined as linear epithelial iron deposition),<sup>[10]</sup> presence of Fuchs spots (defined as discrete, small white-colored flecks consisting of pterygia epithelial cells mainly present in the leading edge).<sup>[11]</sup> Grading system used to assess pterygium morphology was as per anatomical position of the abnormal fibrovascular head (Grade 1: between the limbus and a point midway between the limbus and pupillary margin; grade 2: pterygium head reaching the pupillary margin; and grade 3: beyond the pupillary margin).<sup>[12]</sup>

Surgery was done under topical anesthesia using 0.5% proparacaine eye drops. The Universal wire speculum was applied to separate the lids. Pterygium body was separated and cut from the underlying sclera, by keeping tenon's capsule intact. Head was separated and dissected from cornea by using crescent knife and Lim's forceps. Area to be covered by conjunctival limbal graft was measured by Castroviejo caliper. Same measurement was done at donor site. Dissection and harvesting of conjunctival-limbal graft were done from supero-temporal area. Harvested tissue was reoriented to cover the bare sclera, keeping in mind that limbal tissues should appose limbus at recipient site too. Subconjunctival injection of 0.3 ml Gentamycin and Dexamethasone was given. Eye was patched and bandaged. Postoperatively antibiotic and anti-inflammatory tablets with antibiotic and steroid drops for 1 week was given.

All the primary pterygium specimens after excision, were placed in 10% formalin and sent for the histopathological assessment. Histopathological parameters were classified into three groups-whether epithelial hyperplasia present/absent; vascularity and fibrosis in the stroma

(Predominant vascularity /Predominant fibrosis / No significant difference); inflammatory cells in stroma (mild perivascular/diffuse). Post-operatively patients were followed up on the 2nd day, 1st week, 4th week, 2nd month, 4th month, and 6th month for recurrence. The results of preoperative morphological and histopathological characteristics of pterygium were then compared and findings were correlated with those having recurrence.

**Fig No. 01:**



### 3. RESULTS:

**Table 1 Demographic Details of patients (n=107)**

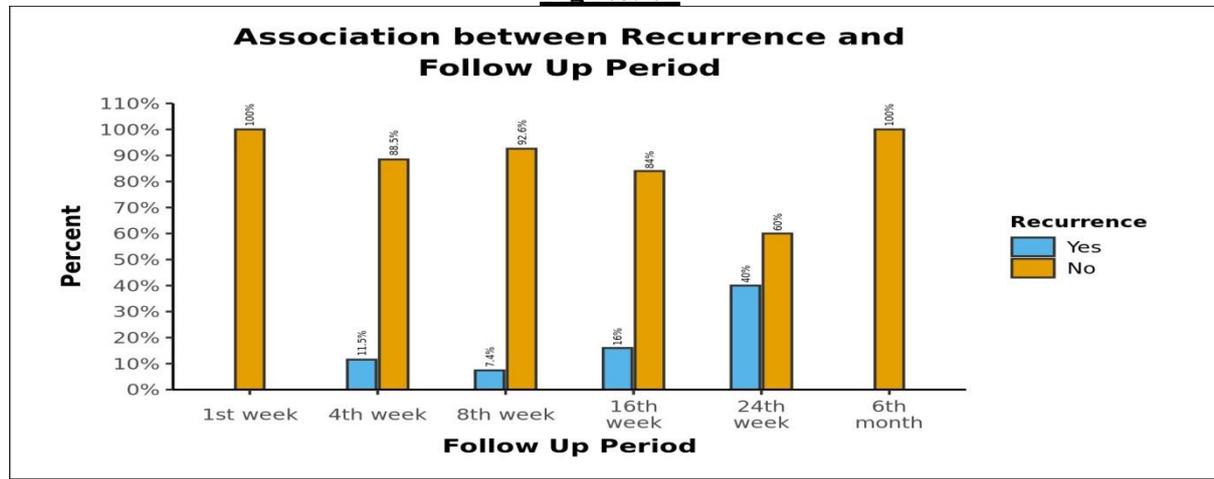
<i>Basic Details</i>	<i>Mean ± SD // Median (IQR) // Min-Max // Frequency (%)</i>
<b>Age (Years)</b>	44.94 ± 13.28 // 45.00 (35.00-55.50) // 21.00 - 70.00
<b>Age</b>	
21-30 Years	19 (17.8%)
31-40 Years	25 (23.4%)
41-50 Years	29 (27.1%)
51-60 Years	16 (15.0%)
61-70 Years	18 (16.8%)
<b>Gender</b>	
Male	46 (43.0%)
Female	61 (57.0%)
<b>Occupation</b>	
Indoor	40 (37.4%)
Outdoor	67 (62.6%)
<b>Eye</b>	
RE	55 (51.4%)
LE	52 (48.6%)
<b>Location</b>	
Nasal	105 (98.1%)
Temporal	2 (1.9%)

**Table 2 Association of Morphological features with recurrence**

Parameters	Recurrence		p value
	Yes (n = 17)	No (n = 90)	
<b>Morphological Grading: Location</b>			0.360 <sup>\$</sup>
Grade 1	0 (0.0%)	5 (100.0%)	
Grade 2	8 (12.9%)	54 (87.1%)	
Grade 3	9 (22.5%)	31 (77.5%)	
<b>Stokers (Present) Line</b>	1 (5.3%)	18 (94.7%)	0.297 <sup>\$</sup>
<b>Fuchs (Present)*** Spots</b>	4 (80.0%)	1 (20.0%)	0.002 <sup>\$</sup>

\*\*\*Significant at  $p < 0.05$ , \$: Fisher's Exact Test

**Fig No. 02**



**Table 3 Histopathological parameters and recurrence**

Parameters	Recurrence		p value
	Yes (n = 17)	No (n = 90)	
<b>HPE: Epithelial Hyperplasia (Present)</b>	16 (43.2%)	21 (56.8%)	0.124 <sup>\$</sup>
<b>HPE: Overwhelms (Present)*** Vascularity Fibrosis</b>	12 (66.7%)	6 (33.3%)	<0.001 <sup>#</sup>
<b>HPE: Vascularity Similar to Fibrosis (Present)</b>	3 (23.1%)	10 (76.9%)	0.315 <sup>\$</sup>
<b>HPE: Fibrosis Overwhelms Vascularity (Present)</b>	3 (18.8%)	13 (81.2%)	0.062 <sup>#</sup>
<b>HPE: Perivascular Stromal Inflammation (Present)***</b>	3 (12.0%)	22 (88.0%)	<0.001 <sup>#</sup>
<b>HPE: Diffuse Stromal Inflammation (Present)***</b>	15 (88.2%)	2 (11.8%)	<0.001 <sup>#</sup>

\*\*\*Significant at  $p < 0.05$ , \$: Fisher's Exact Test, #: Chi-Squared Test

The data was entered into the excel sheet. The analysis was done using SPSS software, 20.0 version, IBM, Chicago. Chi-Square test, unpaired t-test, Mann Whitney U test, Wilcoxon signed rank test and Fischer exact test were employed to establish association between different variables. p-value  $< 0.05$  was considered statistically significant. Table 1 depicts demographic details of patients showing mean age, female and male population, occupational details, eyes involved, and site of pterygium. Table 2 shows association morphological grading with recurrence of pterygium. Stocker's line was present in 19 patients (all were having stationary type of pterygium), out of which only 1 patient had recurrence. Fuchs spots was seen in only 5.7 % of patients. Table 3 shows correlation between histopathological findings and recurrence. The following variables were significantly associated ( $p < 0.05$ ) with the variable 'Recurrence': Age (years), Fuchsspots, Higher relative vascularity and Diffuse Stromal Inflammation on histopathology. Figure 1 depicts histopathology slide (40x magnification) of pterygium showing diffuse stromal inflammation, fibrovascular collagen tissue. Out of 107 patients, 17 patients (15.9%) had recurrence. Association of follow up period was also found to be significantly associated and maximum recurrence was reported at 24<sup>th</sup> week follow up visit as shown in Figure 2.

#### 4. DISCUSSION:

Pterygium is a common ocular condition being worldwide in distribution. As the management of pterygium remained unsettled it presents a challenge to the current ophthalmic surgeons, mainly because of its regrowing tendency despite many medical and surgical treatment options. Our study showed a high pterygium incidence in 40 + years, similar to previous study.<sup>[9]</sup> In our study risk ratio of primary pterygium between female: male was 1:3. Since our study population contained participants coming from low socioeconomic backgrounds and in these communities females were commonly occupied in outdoor work, this might be a reason for an increased number of female pterygium cases in our study. This finding was contrary to the previous available literature, however, study by Hua Zhong et al supported this finding.<sup>[10]</sup>

In our study higher incidence of primary pterygium was seen among outdoor workers, previous studies supported this study.<sup>[9]</sup> However, this finding might be biased because our study population had patients from lower socioeconomic background, who mainly work in outdoor environment. Pterygium is more commonly located nasally. In our study, 93% of pterygia were located nasally whereas only 7% were temporal. Almost same findings have been reported by Lin *et al.*, which showed that 98.68% of the study group had pterygium located on the nasal side.<sup>[11]</sup> Nasal predominance of pterygium might be due to total internal reflection of light and two anterior ciliary arteries on the nasal side & tear pooling.<sup>[12],[13]</sup> In our study, stockers line was seen in all stationary type of pterygium and also it was found to be significantly associated with grade 1 thickness of pterygium.

Fuchs spots might represent precursor lesions to UV-associated ocular surface pathology, associated with high inflammatory activity and recurrence. In our study, it was found to be significantly correlated with recurrence similar to previous study and found in only 5 recurrence cases out of 17. Since its ideal examination is done by in vivo confocal microscopy, therefore many findings might have been missed on slit lamp.<sup>[15]</sup> In our study, recurrence was seen in 15.88% of patients in 6 months follow-up after CLAU surgery, and in previous studies recurrence rate varied from 3%-30%.<sup>[16],[17]</sup> Our study concluded that younger age group (21-40 years) was found to be significantly associated with recurrence, this might be due to higher inflammatory activity of pterygium tissue in younger age

group.<sup>[18]</sup>Sang Beom et al also found morphological factors and vascularity factors on impression cytology to be associated with higher risk of recurrence.<sup>[19]</sup>In our study also, higher relative vascularity, and diffuse inflammation on histopathological examination were found significantly associated with recurrence. These findings supported that apart from degenerative factors, proliferative activity also contribute in pathogenesis of recurrent pterygium. However, other studies showed that there was no significant difference between primary and recurrent pterygia in histopathological features.<sup>[20],[21]</sup> In our study occupation, laterality, and location of pterygium were found not to be related to recurrence.

## 5. CONCLUSION:

Out of our observation and discussion with the currently available literature, we have come to the conclusion that Fuchs spots, higher vascularity and stromal inflammation are the leading contributing factors in the recurrence of pterygium. This indicated that histopathological examination of excised tissue can be used to forecast patients (especially younger ones) having higher tendency towards recurrence, which will definitely help in its early management. This also suggested role of vascular growth factors and inflammatory cytokines in the pathogenesis of recurrent pterygium, although we didn't compare histopathological parameters of primary and recurrent pterygium in our study, as histopathological samples of only primary pterygium were sent. As per these findings of our study, we can also prevent postoperative recurrence by controlling pre-operative inflammation and vascularity by giving steroids or cyclosporine pre-operatively, although this is a matter of further study.

### Key message:

Fuchs spots, red and fleshy pterygium, younger patient along with more vascularity and diffuse inflammation on histopathological examination can be a tell-tale sign of postoperative recurrence. So, patients having these pre-operative features should be followed up strictly.

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