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## Original Research Article

## Periocular and orbital amyloidosis: A case series study

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## ABSTRACT

**Purpose:** To present the demographic and clinical profile and management strategies of patients with periocular and orbital amyloidosis.

**Materials and Methods :** This study retrospectively reviewed the clinical records of twelve patients with periocular and orbital amyloidosis between January 2011 and February 2019 in Bangladesh. Clinical evaluation and Imaging studies were helpful to diagnosis the patients, but surgical biopsy followed by histopathological study was done to confirm the diagnosis. All cases were investigated to rule out systemic amyloidosis with limited facility and no systemic involvement was found. Informed written consent for surgical procedure and Clinical photographs were taken for all patients for documentation and clinical research.

**Results:** The study included thirteen patients including nine male (69.2%) and four female (30.8%) patients. Among the patients, seven (53.8%) were unilateral and six (46.2%) were bilateral. Clinical signs and symptoms were visible or palpable periocular mass or tissue infiltration in all 13 (100%) cases, mechanical ptosis was observed in 6 (46.2%) cases, and proptosis or globe displacement was found in 4 (30.8%). Age ranges from 25 years to 65 years. The Mean age  $\pm$  SD was  $48.23 \pm 10.64$  years. Treatment modalities were mainly open surgical biopsy either excision (53.8%) or debulking (46.2%).

**Conclusions:** Periocular and orbital amyloidosis may present with a wide spectrum of clinical findings depending on the location of the disease. The goal of treatment is to preserve function and to prevent sight-threatening complications.

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## 1. Introduction

Amyloidosis is a progressive, diverse, heterogenous disorders involving the deposition of hyaline extracellular

abnormally folded proteins in the various tissues throughout the body including the orbit and periocular tissues which ultimately causes tissue destruction.<sup>1-3</sup> The clinical presentation classified by the clinicopathological features, the disease locations and magnitude of amyloid deposits.<sup>4</sup> Localized amyloidosis involves only one organ, but

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systemic amyloidosis usually involves multiple organs. The International Society of Amyloidosis has described a four subtypes classification system based on clinical presentation: Primary localized amyloidosis (most common), Primary systemic amyloidosis, Secondary localized amyloidosis, Secondary systemic amyloidosis.<sup>5</sup> Primary localized amyloidosis is usually benign and has got no effect on survival. As periocular and orbital amyloidosis is usually benign and rare, definitive diagnosis is often delayed due to lack of suspicion.<sup>6,7</sup>

The usual pattern of amyloid deposition of Ocular and periocular tissues in multiple compartments, including the adnexa, extraocular muscles, levator palpebrae muscle, conjunctiva with infiltration around blood vessels and extension posteriorly in tenon's capsule, cornea, lens and capsule, anterior uvea and trabecular meshwork, as well as vitreous and retina.<sup>2,4</sup> This deposition of amyloid material in the periocular and orbital tissues presenting the following clinical features ptosis, proptosis, globe displacement, motility disturbances, firm/non tender palpable mass.<sup>8</sup> Amyloidosis disrupts tissue structure and impairs function. If major organs like kidney or heart are involved, the consequences can be fatal.<sup>9,10</sup> As the clinical diagnosis of amyloidosis can vary immensely. So, classic histopathological study plays an important role for definitive diagnosis.<sup>1</sup> The binding of Congo red dye in addition of apple-green birefringence on polarized light microscopy is used as the gold standard for the diagnosis of amyloidosis.<sup>11</sup> Here, we are attempting to describe the demographic and clinical pattern, and surgical strategies of the patients with periocular and orbital amyloidosis.

## 2. Materials and Methods

A retrospective case series was carried out in three tertiary eye hospitals including Sheikh Fazilatunnesa Mujib Eye Hospital and Training Institute, Bangladesh Eye Hospital and Institute, and Harun Eye Hospital in Bangladesh from the January 2020 to December 2020. This study reviewed all the histopathological confirmed diagnosed patients with periocular and orbital amyloidosis who attended and followed from January 2013 and December 2019. We reviewed the clinical records of these patients: demographic data, location of the disease, the histopathological result, treatment modalities. All patients were evaluated through clinical examination, and imaging studies for diagnosis, but surgical biopsy followed by histopathological study was done to confirm the diagnosis. The follow-up period was recorded up to 6 months of the surgery. All cases were investigated to rule out systemic amyloidosis with limited facility and no systemic involvement was found. Informed written consent for surgical procedure and Clinical photographs were taken for all patients for documentation and clinical research.

## 3. Results

A total of thirteen patients were evaluated in this study. Out of twelve, nine (69.2%) patients were male and four (30.8%) were female patients [Table 1]. There were seven (53.8%) unilateral, and six bilateral (46.2%) involvements of periocular and orbital amyloidosis. Among the unilateral cases, right (57%) periocular area and left (43%) site was involved in this study.

The mean age  $\pm$  SD was  $48.23 \pm 10.64$  years, and the median age was 49 years with age ranges from 25 years to 65 years. The 95% of CI was from 40.80 to 54.66. All cases were confirmed by the diagnosis of amyloidosis by open surgical biopsy followed by histopathological confirmation. The most clinical feature was visible or palpable periocular mass or tissue infiltration that was found in all 13 (100%) cases. Others clinical features include mechanical ptosis, proptosis or globe displacement, and restricted ocular motility [Table 2].

The most common periocular involvement was eyelid (84.6%), followed by orbital tissues (61.5%), lacrimal gland (30.7%), and conjunctiva (23%) [Table 3]. Treatment modalities were mainly open surgical biopsy either excisional biopsy (53.8%) or debulking (46.2%) of the tissues. After the histological confirmation of amyloidosis, all patients were treated by oral corticosteroids as 0.5 mg/kg/body weight with tapered doses and maintaining a low dose up to 2 months depending on physical conditions of the patients. The progression of the disease was observed in 2 (15.4%) cases, and 84.6% cases were stable up to 6 months of follow up time.

## 4. Discussion

Periocular and Orbital amyloidosis is rare, commonly slow progressive, localized and associated with primary benign disease.<sup>12,14–16</sup> Periocular and Orbital amyloidosis is seen most in the eyelid, followed by the orbit, conjunctiva, and lacrimal gland. Localized amyloidosis can have a recurrent and varied presentation.<sup>13</sup> Lacrimal gland may involve unilaterally or bilaterally.<sup>15</sup> The deposition of Amyloid protein in the levator palpebrae muscle causes ptosis and may present with other orbital or conjunctival signs.<sup>17</sup> In our study, we present a case series of thirteen patients with periocular and orbital amyloidosis. We collected data of patients over a period of 7 years. In this study, out of thirteen, nine (69.2%) patients were male and four (30.8%) were female. The mean age  $\pm$  SD was  $48.23 \pm 10.64$  years, with age ranges from 25 years to 65 years. Clinical presentations were visible or palpable periocular mass or tissue in all cases, The most common lesion in the eyelid (84.6%).

In a collaborative review, Leibovitch I et al<sup>12</sup> study included 24 patients (62.5% female, 37.5% male) with the mean age of 57 years. The gender distribution of is

**Table 1:** Demographic and clinical profile of study patients

Case No.	Age/ Gender	Laterality	Clinical manifestations	Mode of Surgery
1.	49Y/M	Right	Conjunctival Mass	Excisional Biopsy
2.	50Y/M	Right	Proptosis, Restricted Ocular motility, Mechanical ptosis, Eyelid and Orbital Palpable mass (Figure 3)	Debulking and Biopsy
3.	40y/M	Left	Orbital and Upper Eyelid mass, Mechanical ptosis, Proptosis, Restricted ocular Motility	Debulking and Biopsy
4.	55y/M	Left	Palpable mass in the left upper eyelid with Mechanical Ptosis (Figure 1)	Excisional Biopsy
5.	50y/M	Right	Eyelid and orbital palpable mass (Figure 2)	Excisional Biopsy
6.	25y/F	Both	Conjunctival growth	Excisional Biopsy
7.	38y/F	Both	Eyelid and Anterior orbital mass, Mechanical ptosis	Excisional Biopsy
8.	57y/F	Both	Bulbar Conjunctival and Eyelid mass	Excisional Biopsy
9.	49y/M	Right	Palpable mass in the Right Lower Eyelid	Excisional Biopsy
10.	43y/M	Both	Proptosis, Eyelid, and orbital palpable mass	Debulking and Biopsy
11.	44y/F	Left	Eyelid and Anterior Orbital mass	Debulking and Biopsy
12.	62y/M	Both	Eyelid and Orbital mass, Mild Proptosis, Mechanical Ptosis, Restricted Ocular Motility	Debulking and Biopsy
13.	65y/M	Both	Eyelid and anterior orbital Mass (Figure 4)	Debulking and Biopsy

**Table 2:** Clinical manifestation of this study compared to other studies.

Clinical sign/ symptoms	Percentages	
	Our Study (N-13)	Other Studies (N-96) <sup>12,13</sup>
Visible or Palpable mass/Periocular Tissue infiltration	N=13 (100%)	N=75 (78.1%)
Mechanical Ptosis	N=6 (46.2%)	N=58 (60.4%)
Proptosis/ Globe Displacement	N=4 (30.8%)	N=15 (15.6%)
Restricted ocular motility	N=3 (23%)	N=8 (8.3%)

**Table 3:** Location of Amyloid deposition

Location of Amyloid deposition	Percentages
Eyelid	N=11 (84.6%)
Orbit	N=8 (61.5%)
Lacrimal gland	N=4 (30.7%)
Conjunctiva	N=3 (23%)



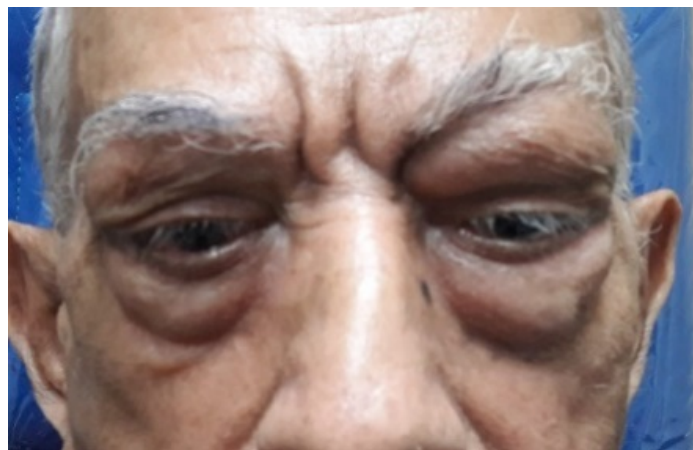
**Fig. 1:** A 55 yrs old male patients presented with left eye ptosis, a mass on supero-temporal aspects of left orbit and left upper eyelid. Patients also complain of foreign body sensation in the left eye. Excision biopsy was performed, and histopathological findings confirm the periocular Amyloidosis. Up to 1 year follow up, no recurrence was observed (Case 4).



**Fig. 2:** A 50-year-old male patients with a mass on supero-temporal aspects of right orbit, and right upper eyelid which cause severe mechanical ptosis. Excision biopsy was done, the lesion involving the right lacrimal gland. Histopathological findings confirm Amyloidosis involves lacrimal gland (Case 5)

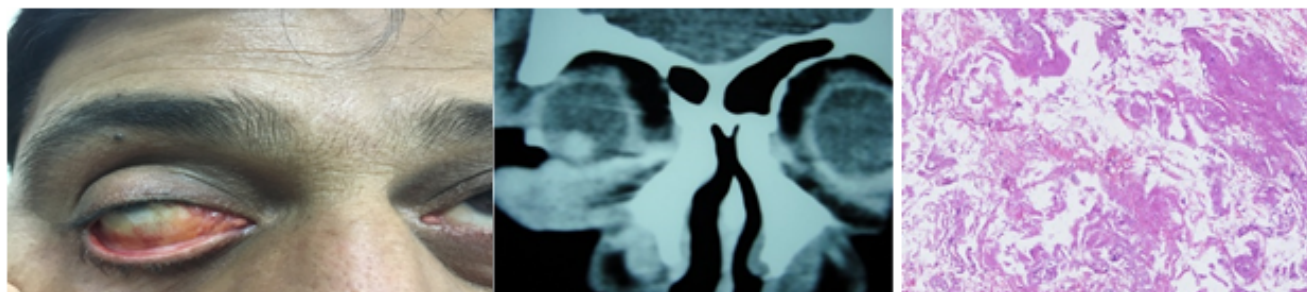


**Fig. 3:** A 50-year-old male presented with a mass on supero-temporal aspects of left orbit and left upper eyelid. Histopathological findings confirm the diagnosis of amyloidosis. Congo red staining was positive.



**Fig. 4:** A 65-year-old male presented with a mass on all eyelids and anterior periorbital area in upper and lower quadrants of both orbits. debulking of the tissues was made as much as possible. Histopathological analysis confirmed the amyloidosis.





**Fig. 5:** A 49-year-old man diagnosed with a deep infiltration of amyloid in right palpebral and bulbar conjunctiva. Histopathological reports confirm Amyloidosis (case 1).

little quite difference from our study. The most common clinical features were Visible or palpable periocular mass or tissue infiltration (95.8%). Others include ptosis (54.2%), restrictive ocular motility (16.7%), and diplopia (8.3%). The clinical presentation of this study is near to similar of other studies [Table 2]. The data from this large case series and our study were similar in clinical presentations. Taban M. et al.<sup>17</sup> reviewed literature on all cases of primary localized orbital amyloidosis till 2004, the age ranges from 15 years to 86 years. Clinically, the most common presentation is a painless, palpable mass. Other presentations were ptosis, proptosis, and globe displacement.<sup>13,17</sup>

The eyelid skin is a common site of amyloid deposition in both primary and secondary amyloidosis. If the lid is affected, it is often found to be associated with systemic conditions.<sup>13,18,19</sup> In contrast, amyloidosis in conjunctiva is often localized with no other associations.<sup>18</sup> Conjunctival amyloidosis is commonly a primary, and localized lesion,<sup>12</sup> but it may represent systemic amyloidosis in some cases.<sup>20</sup> Though in our study, all cases were investigated to rule out systemic amyloidosis with limited facility and no systemic involvement was found. Primary eyelid amyloidosis is a rare clinical entity that often leads to misdiagnosis.

Lacrimal gland involvement with amyloid is uncommon.<sup>3,10,11</sup> Lacrimal gland deposition with amyloid in primary localized orbital cases is usually unilateral, whereas systemic cases tend to be bilateral.<sup>11</sup> In our series, there was one case with unilateral lacrimal gland involvement: with no underlying systemic disease. Usually in focal orbital amyloidosis, amyloid deposits are visible in eyelid or conjunctiva and in superior portions of orbit.<sup>14</sup> Computed tomography are not diagnostic but are important in localizing the involved orbital structures.

Extraocular muscle infiltration is highly variable with presentations of proptosis (unilateral or bilateral), diplopia, or restrictive ocular movement.<sup>21,22</sup> A study reported on enlargement of extraocular muscle on CT interpretation in 24 cases of periocular amyloidosis.<sup>12</sup> A total of three (25%) cases presented with restrictive ocular motility in our case series, and extraocular muscles were involved in 5 cases

(41.7%).

Orbital imaging (CT scan / MRI) is needed to assess the extent of periocular infiltration in all cases of ocular adnexal amyloidosis.<sup>18</sup> Orbital imaging modality cannot differentiate between amyloid and soft tissue lesions.<sup>12</sup> CT Scan of the orbit was advised in all orbital involvement of disease process in our study. CT scan found most of the cases suggest hematomalymphoid tumours, Chronic inflammatory lesions, hemangioma, but the histopathological confirmation was the definitive diagnosis.

The amyloidosis presents diversity in clinical conditions and commonly required a tissue sample for stained with Congo red or thioflavin compounds, followed by the definition of the fibril protein using the IHC-based techniques. These techniques are quite well applicable in clinically significant amyloid diseases.<sup>23</sup>

Amyloidosis may infiltrate the ocular tissues like trabecular meshwork, uveal tissue, vitreous, and retinal pigment epithelium which leads to amyloid related secondary glaucoma, amyloid vitreous opacity, and amyloid retinal deposits.<sup>24,25</sup> Among the 68 patients of systemic amyloidosis, nine patients were presented with ocular morbidity. Eight patients were associated with ocular and adnexal involvement like conjunctiva, extra ocular muscles, trabecular mesh work, temporal artery, and cranial nerve amyloid deposition. One patient was associated with amyloid related corneal dystrophy.<sup>26</sup>

Treatment modalities are usually observation and surgical excision or debulking. A total of 21% of cases showed significant progression following treatment, whereas 79% showed stable or no recurrence after treatment.<sup>12</sup> The treatment modalities depend on the location of disease, functional defect, and cosmesis. In this study treatment modalities include mainly excisional biopsy (53.8%), and surgical debulking (46.2%) of the lesions followed by histopathological confirmation. Progression of the disease was observed in 2 (15.4%) cases during follow-up time. A study reported a 27% recurrence rate after surgical debulking of conjunctival amyloidosis.<sup>20</sup> Recently a study mentioned that the use

of liquid nitrogen cryotherapy is safe and effective for conjunctival amyloidosis.<sup>27</sup> The main aim of the management would be to preserve ophthalmic function and prevent vision threatening complication as well as associated manifestations like ptosis, strabismus. Total surgical excision is often difficult because of its diffuse infiltrative nature. Although the local recurrences are common, a long-term ophthalmic follow-up is recommended for all patients with diagnosed or suspected ocular and adnexal amyloidosis. Close collaboration between the ophthalmologist and the internist will facilitate a more precise diagnosis of ocular and systemic involvement in amyloidosis.<sup>12,27</sup>

In our study, we failed to demonstrate plasma protein electrophoresis, bone marrow biopsy, abdominal fat biopsy to detect the systemic manifestations due to limited facilities.

## 5. Conclusion

A mass lesion was the most common symptom. Amyloidosis can only be confirmed by biopsy. Systemic disease must be ruled out. Complete surgical excision is not feasible in many cases, and the majority respond to simple debulking and excision biopsy.

## 6. Conflict of Interest

The authors declare no relevant conflict of interest with respect to research, authorship and or publication of this article


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None.

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