# **Original Research Article**

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# A clinical study of primary cutaneous localized amyloidosis

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#### **ABSTRACT**

**Background:** Amyloidosis refers to abnormal extracellular tissue deposition of one of the biochemically unrelated proteins that share certain characteristic staining properties such as apple green birefringence of congo red stained preparations under polarized light. Amyloid deposition may occur in many organs of the body (systemic amyloidosis) or may be restricted to one tissue site (localized amyloidosis).

**Methods:** Observational study was conducted in the Department of Dermatology, Narayana Medical College and Hospital, Nellore. In this study of 70 patients a complete history and clinical data was taken including details of presenting complaints, age, site, duration, course of the disease was recorded. Special importance was given to the friction history using different scrubs, family history and photo exposure.

**Results:** Out of 70 patients of cutaneous amyloidosis 55 patients (78.6%) were of macular amyloidosis. Male:female ratio was 1:2.3. Majority of the patients were housewives (42.8%) and 28.5% of agriculturists. Majority of the patients (40) with cutaneous amyloidosis had disease duration between 2-5 years. In 70 patients of cutaneous amyloidosis 64.3% were symptomatic. 92% patients give history of using scrub. 50% of patients had history of photo exposure. Positive family history was seen in 7 patients (10%) and most common site involved was extensor aspect of arm.

**Conclusions:** From our study it can be concluded that cutaneous amyloidosis is more common among females, most patients are symptomatic, majority have history of using scrub and photo exposure and most common site involved is extensor aspect of arm.

Keywords: Cutaneous amyloidosis, Lichen amyloidosis, Biphasic amyloidosis

# INTRODUCTION

Amyloidosis refers to abnormal extracellular tissue deposition of one of the biochemically unrelated proteins that share certain characteristic staining properties such as apple green birefringence of congo red stained preparations under polarized light. Amyloid deposition may occur in many organs of the body (systemic amyloidosis) or may be restricted to one tissue site (localized amyloidosis). Localized or organ limited amyloidosis can be classified into cutaneous amyloidosis, cerebral amyloidosis and endocrine amyloidosis. Primary localized cutaneous amyloidosis (PLCA) refers to

deposition of amyloid in apparently normal skin with no evidence of deposits in internal organs.<sup>2</sup>

PLCA is classified into three categories: macular amyloidosis, lichen amyloidosis and nodular amyloidosis. Macular amyloidosis is characterized by dark brown pigmentation in rippled pattern predominantly over the upper back, arms and forearms. Whereas lichen amyloidosis is present as persistent pruritic papular lesions predominantly over lower limbs. Nodular form of amyloidosis is a rare type which is characterized by single or multiple nodules of size 1-3 cm present usually on legs or face.<sup>3</sup>

Etiopathogenesis of cutaneous amyloidosis is poorly understood. PCLA appears to be multi factorial in origin, only environmental and genetic factors appear to play an important role in pathogenesis. The keratinocyte degeneration mechanism might be due to chronic friction which is caused by coconut fibers, pumice stone and nylon bath sponges.<sup>4</sup>

Histopathology shows amyloid deposits confined to papillary dermis in popular and macular forms of PLCA whereas dermis, subcutis and blood vessel walls are diffusely infiltrated with amyloid in nodular forms. Most cases of PLCA remain chronic and difficult to treat. Topical glucocorticoids, intralesional steroids, dermabrasion and topical retinoids have been used with success.<sup>4</sup>

PLCA is a commonly seen problem in our scenario. As there are less studies on this subject, a clinical study was done to make an insight into the etiological factors involved in PLCA, and the comparison of age and sex distribution in PLCA.

# **METHODS**

This study was conducted in the Department of Dermatology, Narayana Medical College and Hospital, Nellore, Andhra Pradesh during the period January 2013 to January 2014.

# Study group

The study group includes 70 clinically diagnosed cases of PLCA attending department of Dermatology.

#### Methods

In all the patients a complete history and clinical data was taken including details of presenting complaints, age of onset, site, duration, course of the disease was recorded. Special importance was given to the friction history using different scrubs, family history, photo exposure and histopathology were patient had given consent.

A complete general systemic examination and detailed cutaneous and type of skin lesions are recorded. Patients willing were subjected for biopsy were sent to the Department of Pathology for a detailed histopathological examination. At the end results were analyzed according to statistical proportion.

# **RESULTS**

Out of 70 patients of cutaneous amyloidosis 55 patients were macular amyloidosis (78.6%), 10 patients were lichen amyloidosis (14.3%) and 5 patients of biphasic amyloidosis (7.1%) were seen (Table 1).

In the present study majority of the patients belonged to age group of 21-30 years (57%) and the next age group

includes 11-20 and 31-40 years (14.3%) and next is age groups of 41-50 and 51-60 years (7.1%). The least effecting age group is 41-60 years forming only 7.1% (Table 2).

Table 1: Distribution according to clinical types (n=70).

Clinical type	No. of patients	Percentage
Macular amyloidosis	55	78.6
Lichen amyloidosis	10	14.3
Biphasic amyloidosis	5	7.1

Table 2: Age distribution in cutaneous amyloidosis.

Age in years	No. of patients	Percentage
11-20	10	14.3
21-30	40	57
31-40	10	14.3
41-50	5	7.1
51-60	5	7.1

#### Sex distribution

Out of 70 patients 70% constituted female population and the rest 30% were males. Male: female ratio was 1:2.3 (Figure 1).

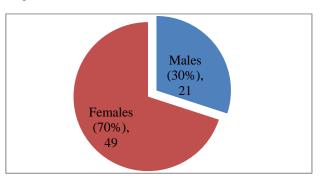


Figure 1: Sex distribution.

In the present study out of 70 patients, 21 were males (30%) and 49 (70%) were females. Out of 55 patients of macular amyloidosis 20 (36.3%) were males and 35 (63.6%) were females. Amongst 10 cases of lichen amyloidosis 1 case was male (10%) and remaining 9 (90%) cases were females. And among 5 cases of biphasic amyloidosis all the 5 cases (100%) were only females and no male cases were reported (Figure 2).

In the present study of cutaneous amyloidosis majority of the patients were housewives (42.8%) and 28.5% of agriculturists and 14.2% of students and others like teachers and office workers (Figure 3).

Majority of the patients with cutaneous amyloidosis had duration between 2-5 years 40 (57.1%). Duration of 6

months to 1 year was observed in 28.5% of cases and 7.1% of cases were observed in patients below 6 months and above 1 year of duration (Figure 4).

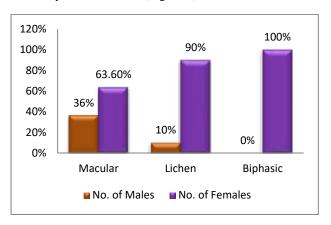


Figure 2: Sex distribution in macular, lichen and biphasic amyloidosis.

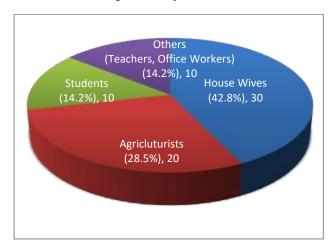


Figure 3: Relation to occupation in cutaneous amyloidosis.

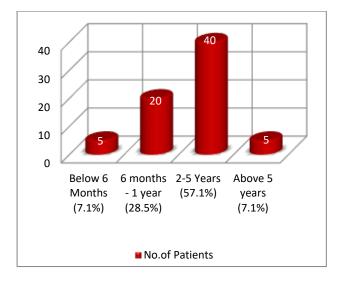


Figure 4: Duration of the disease in cutaneous amyloidosis.

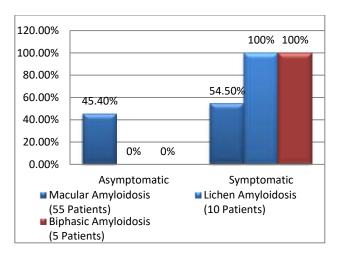


Figure 5: Symptoms.

In 70 patients of cutaneous amyloidosis 64.3% were symptomatic and 35.7% were asymptomatic. In macular amyloidosis 25 (45.4%) patients were asymptomatic and 30 (54.5%) were symptomatic. And in both lichen and biphasic amyloidosis 100% were symptomatic (Figure 5).

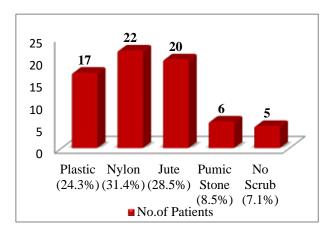


Figure 6: History of friction (scrub).

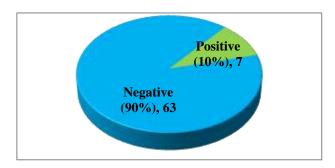


Figure 7: Family history in cutaneous amyloidosis.

In this study of 70 patients 92% gives history of using scrub. Maximum patients used nylon scrub (31.4%) followed by jute (28.5%) then plastic scrub (24.3%) and pumice stone (8.5%). 7.1% did not give history of scrub (Figure 6).

In primary cutaneous amyloidosis positive family history was seen in 7 patients (10%) and 63 patients (90%) gave negative family history (Figure 7).

# Photo exposure

Out of 70 patients of cutaneous amyloidosis 50% of patients had history of photoexposure and remaining 50% had no photoexposure history (Figure 8).

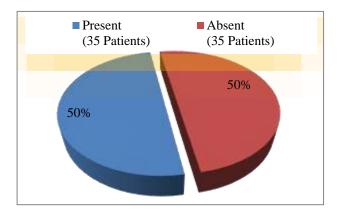


Figure 8: Photo exposure.

Pigmented macules with rippled pattern was seen in all cases of macular amyloidosis. Pigmented hyperkeratotic papules were seen in all cases of lichen amyloidosis and biphasic amyloidosis. Lichenification was seen in all cases 100% of lichen and biphasic amyloidosis. In macular amyloidosis lichenification was seen in 5 (9%) of cases (Figure 9). Most commonly involved site in cutaneous amyloidosis was extensor aspect of arm (EAA) 85.7% and most commonly seen in macular amyloidosis followed by anterior aspect of leg (ASL) 28.5% and then extensor aspect of forearm (EAF) and then upper back (UB) 17.14% and last was thigh 7.1% (Figure 10).

# Histopathological findings

In this study of 70 patients only 5 patients gave consent for biopsy. The epidermal changes seen in lichen amyloidosis were irregular acanthosis, hyperkeratosis, and elongation of rete ridges. Hyper granulosis was seen in 1 patient. The dermis showed eosinophilic nodules of amyloid occupying the papillary dermis. These nodules were intensely positive by congo red stain and showed a characteristic apple green birefringence under polarization which was diagnostic of amyloid.

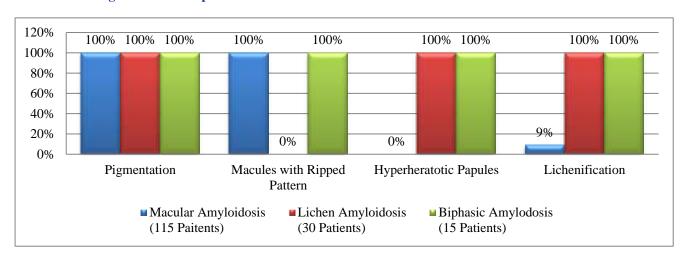


Figure 9: Morphology of lesions.

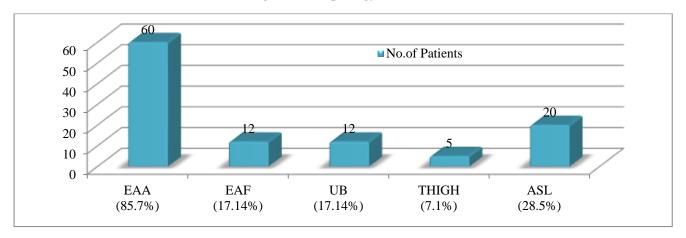


Figure 10: Sites involved in cutaneous amyloidosis.

#### **DISCUSSION**

## Clinical types

In this study, out of 70 cases of cutaneous amyloidosis, 55 (78.6%) were of macular amyloidosis, 10 (14.3%) were of lichen amyloidosis and 5 (7.1%) were of biphasic amyloidosis.

In Saudi Arabia in the year 1997 by Al-Ratrout and Satti conducted a clinicopathological study and they reported that 90% of the cases were macular amyloidosis while only 10% were lichen amyloidosis.<sup>5</sup> Kibbi and Rubeiz in their study found macular amyloidosis in 74.13% of the patient and lichen amyloidosis in 25.86%.<sup>6</sup>

In 1997, Looi studied cases of PLCA in Malaysians and he observed that only 26% were macular mayloidosis while 74% were lichen amyloidosis.<sup>7</sup>

Hence, the occurrence of macular amyloidosis being for commoner than lichen amyloidosis in the present study is in concurrence with the study of Al-Ratrout and Satti, as well as Kibbi and Rubeiz. This study is not in concordance with the study by Looi.

## Age

In the present study, cutaneous amylidosis was more common in the age group of 21-30 years (57%) followed by 31-40 years (14.3%) and similar in 11-20 years (14.3%). The age groups of 41-50 years and 51-60 years had 5 patients (7.1%). The mean age in the present study was 28.9 years.

In the year 1997, Al-Ratrout and Satti observed in their study that cutaneous amyloidosis was commonest in the age group of 31-40 years (28.57%) closely followed by 41-51 years (23.81%).<sup>5</sup> In year 1998, Ozkaya-Bayazit et al observed that majority of the patients of cutaneous amyloidosis belonged to the age group 41-50 years (38.46%) closely followed by 31-40 years (30.77%). The mean age of cutaneous amyloidosis was 43.8 years.<sup>8</sup>

Looi in his study noted cutaneous amyloidosis commonly affected the age group of 30-39 years (29.41%) followed by 20-29 years (24.71%). The mean age of cutaneous amyloidosis was 39 years.<sup>9</sup>

In 2005, Salim et al studied the mean age of cutaneous amyloidosis in this study (28.9 years) cannot be compared to the above studies with majority of the patients in their third decade.<sup>10</sup>

## Sex

In the present study of 70 patients of cutaneous amyloidosis, 21 were males (30%) and 49 (70%) were females, with a male to female ratio was 1:2.3.

Ozakaya-Bayazit et al in their study of cutaneous amyloidosis observed that 15.38% were males and 84.62% were females with a male to female ratio of 1:5.5.8

In the study of Looi, 36.47% were males and 63.53% were females in patients of cutaneous amyloidosis with male to female ratio of 1:1.75.9

A1-Ratrout et al in their study observed that 42.8% of cutaneous amyloidosis were males and 57.14% were females with a male to female ratio of 1:1.33.5

Kibbi et al in their study observed that 29.31% were males and 70.69% were females with a male to female ratio of 1:2.4.6

In this study, male to female ration of cutaneous amyloidosis is 1:2.3 correlated with studies of Kibbi and Rubeiz.

## **Occupation**

Majority of the patients of the study were housewives (42.8%), followed by agriculturists (28.5%) and students and other (teachers and officers) 10% each.

Tay et al in their study of cutaneous amyloidosis observed that 42.5% were housewives followed by 37.5% of laborer's. <sup>11</sup> Professionals and clerks formed 10% each.

## Duration

Majority of the patients with cutaneous amyloidosis had duration between 2-5 years (57.1%). Duration of 6 months to 1 year was seen 28.5% of the patients, 7.1% of patients had duration more than 5 years and duration less than 6 months each.

Al-Ratrout et al in their study found that in cutaneous amyloidosis the duration varied from 1 year to 20 years with a median of 8 years.<sup>5</sup>

Black et al in their study of cutaneous amyloidosis observed that the shortest duration was 2 months and longest 31 years with an average of 11 years.<sup>12</sup>

In the present study, unlike the majority of the studies many patients came forward for treatment within the first 2 years of onset of the disease. This could be attributed to the fact that majority of the patients were house wives and hence came forward for treatment because of cosmetic awareness. Majority of patients in this study had itching, which might be another reason why they came earlier for treatment.

#### **Symptoms**

Out of 100 patients with cutaneous amyloidosis, 64.3% were symptomatic and 35.7% were asymptomatic.

Tay et al in their study of cutaneous amyloidosis observed that 62.5% had itching whereas 37.% were asymptomatic. <sup>11</sup> Kibbi and Rubeiz in their study found that 77% had pruritis. <sup>6</sup> A1-Ratrout et al in their study found that 71.43% had pruritis while 28.57% were asymptomatic. <sup>5</sup> Black et al in their study of cutaneous amyloidosis observed that 80.95% were asymptomatic. <sup>12</sup>

#### History of friction

In this study of 70 patients, 65 (92%) gives history of using scrub. Maximum patients used nylon scrub (31.4%), followed by jute scrub (28.5%), plastic (24.3%) pumice stone (8.5%) and 5 (7.1%) did not give scrub history. Salim et al in their study of cutaneous amyloidosis reported that 56.7% of the patients had positive scrub history. <sup>10</sup> In the year 1993, Sumitra et al studied the role of scrub in 65 patients and found that in 30.76% of the patients, friction factory could be attributed in the etiology of cutaneous amyloidosis. <sup>13</sup> Rasi et al in their study on macular amyloidosis reported that use of back scratchers, nylon towels of vigorous rubbing of the skin was positive in only was limited to 4%. <sup>14</sup>

In this study, majority of the patients showed positive scrub history comparable with the reports of Salim, but not in concordance with studies by Rasi et al which reported scrub history in few patients only. Scrubbing while taking bath is a very common practice in this part of the country. This could be the reason for variations seen in western and South Indian studies.

## Photo exposure

In this study, history of photo exposure is seen in 50% of patients and remaining 50% of patients had no photo exposure history. These results were in concordance with the studies by Black et al who reported the role of photo exposure in the causation of cutaneous amyloidosis, but not consistent with the studies of Rasi et al.<sup>14</sup>

#### Family history

In primary cutaneous amyloidosis, positive familial history was recorded in 7 patients (10%) and 90% of the patients showed negative family history.

In 2005, a study on lichen amyloidosis by Salim et al showed that 20% of the patients had positive family history. Taheri studied 100 cases of cutaneous amyloidosis and reported that 10% of patients had positive family history. Dzkaya-Bayazit et al in their study observed that no patient gave a family history of similar complaints. Black and Jones also did not report any family history in their study. Al-Ratrout et al in their study found that 4.76% had a positive family history.

A positive family history of 10% seen in this study can be supported by observation made by Salim et al that genetic

predisposition and racial factors may contribute to the occurrence of primary cutaneous amyloidosis.<sup>10</sup>

#### Morphology of lesions

A1-Ratrout et al in their study observed confluent macular pigmentation in 42.86%, rippled pattern of pigmentation in 23.81%, papules and hypopigmentation in 10% each.<sup>5</sup> Black and Jones in their study of macular amyloidosis observed that in 57.14%, the predominant lesion was macules.<sup>12</sup> Rippled pattern was found in 42.86%. The present study pigmented macules with rippled pattern were seen in all (100%) cases of macular amyloidosis.

In our study we observed pigmented hyperkeratonic papules in all (100%) cases of lichen amyloidosis and biphasic amyloidosis which is in concordance with study by Salim et al and Ozkaya-Bayazit et al who reported hyperpigmented hyperkeratotic papules and pigmentation in all cases of lichen amyloidosis. 8,10 Tay et al in their study of lichen amyloidosis observed that 67.5% had papules, 22.5% had plaques 7.5% had macules and 2.5% had nodules. 11

## Site of involvement

All patients had involvement of more than one site. Most commonly involved site was EAA (85.7%), followed by UB (30%), EAF (24%), and lower leg (20%).

Black et al in their study of cutaneous amyloidosis found that upper arms and upper back were involved in 33.33% each. Thigh and lower legs were affected in 14.29% each. Shoulders and back were involved in 54.14% each while forearms were affected in 19.05% Ozakaya-Bayazit et al in their study found involvement of upper back in 80% arms, scapular area and trunk were involved in 12% Ortiz-Romero in his study found that all patients had lesion on the back (100%).

Kibbi et al in their study appreciated lesions over the upper back in all the patients (100%). Arms were involved in 27.91% while neck and legs were involved in 9.3% each. Face was involved in 4.65% whereas abdomen and thighs were involved in 2.33% each.<sup>6</sup>

#### Histopathology

Salim et al showed in their cases, epidermal changes of hyperkeratosis in 100% of their cases, acanthosis in 9% of the cases, papilomatosis in 33.3% of the cases, hypergranulosis in 16.7% of the cases and elongation of the rate ridges seen in 13.3% of the cases. Amyloid deposits were detected in 28 out of 30 patients. The present study however showed in biopsied cases of lichen amyloidosis-hyperkeratosis and irregular acanthosis. Hypergranulosis was seen in 1 of the patient. Irregular acanthosis and increased granular layer was observed by Browstein and Helwig et al in their study. Amyloid deposition was however seen in the dermis as has been

observed. The clue to final diagnosis and differentiation from their lesion rests in apple green birefringence under polarized light on congo red staining.

#### **CONCLUSION**

From our study it can be concluded that cutaneous amyloidosis is chronic disease more common among females, more common in 2nd and 3rd decade of life, most patients are symptomatic, majority have history of using scrub, many patients had photo exposure and most common site involved is extensor aspect of arm. So our study helps to understand etiological factor and distribution of disease.

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