

# Secondary Renal Amyloidosis: A Prospective Study of Biochemical and Morphological Correlation

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The records of 26 patients out of a total of 38 cases of bilateral pulmonary tuberculosis were scrutinised in order to correlate the clinical features and biochemical alterations with the severity of renal histological lesions. The extent of amyloid deposits was graded from 0 to 4. No correlation was found between the clinical biochemical and severity of renal amyloidosis.

**Key Words:** Amyloid,

Amyloidosis is a generic term for a heterogeneous group of disorders caused by extra cellular deposition of a protein in a characteristic abnormal fibrillar form.<sup>1</sup> Reactive systemic amyloidosis (AA) occurs in association with chronic infections, long-standing inflammatory disorders of unknown aetiology and malignant neoplasms<sup>2</sup>. Tuberculosis remains an important worldwide cause of reactive amyloidosis.<sup>3</sup> The comparative clinical, biochemical, and pathological examination of internal organs of tuberculous patients by biopsy technique helps in the diagnosis of amyloidosis in patients with tuberculosis of lung and pleura<sup>4</sup>. The common presenting features in cases of reactive renal amyloidosis are proteinuria, nephrotic syndrome and renal failure<sup>1</sup>. The proteinuria and nephrotic syndrome in renal amyloidosis is related to the deposition of amyloid in the capillary wall and mesangium<sup>5</sup>. The prognosis of patients with reactive systemic amyloidosis depends on the nature of the underlying disorder which may affect the rate of amyloid progression and survival of the patients is often one to five years after diagnosis<sup>2</sup>.

The present study aims at correlating the degree of proteinuria, abnormalities of serum proteins, and functional impairment by levels of blood urea and creatinine clearance in patients with chronic history of pulmonary tuberculosis with the histological lesions in the renal amyloidosis.

## Materials and Methods

All the thirty-eight patients of present study were admitted in Gulab Devi Hospital and selection criteria were chronic (i.e. more than two years) history of pulmonary tuberculosis and having 2+ or more albuminuria. The diagnosis of renal amyloidosis was confirmed by needle biopsy in all of the patients. Renal biopsies were performed using a disposable true-cut biopsy needle. Routine paraffin blocks were prepared. The serial sections were stained with Hematoxylin and Eosin, Congo red, Periodic Acid Schiff's reaction, and Methanamine silver.

Biochemical investigations were aimed at establishing the cause of renal amyloidosis and for assessing the renal involvement. Blood urea, serum creatinine, total serum proteins, serum albumin, albumin globulin ratio, twenty-four hours total urinary proteins, and creatinine clearance was estimated using standard biochemical procedures.

## Results

### Baseline Studies

#### Age

The ages of these thirty-eight patients ranged between 18 and 70 years. The duration of predisposing illness i.e. pulmonary tuberculosis varied between 2 and 12 years.

Table I: Analysis of serum urea, creatinine, creatinine clearance in 38 cases of bilateral pulmonary tuberculosis

Group	Urea	n=	Creatinine Level (Mg/Dl)	n=	Creatinine Clearance (Ml/Min)	n=
1	20-45(normal)	30(79.0%)	0.7-1.2(normal)	24(63.0%)	160-80(normal)	25(65.8%)
11	46-80(abnormal)	8 (21.0%)	1.3-4.0(abnormal)	14 (37.0%)	79-40(abnormal)	13(34.2%)

### Biochemical Abnormalities

The range of Blood urea, serum creatinine, and creatinine clearance are given in Table I.

Serum proteins varied between 3.7gms/dl and 7.8 gms/dl. Maximum number of cases i.e. 19 had serum proteins between 5.1 and 6.0gms/dl with albumin between 2.0 and 3.8gms/dl and albumin/globulin ratio 0.9 and 2.7.

Twenty-four hours urinary proteinuria ranged between 3.6 and 28 grams. It was less than 5g/24hrs in 6 patients and more than 5.5g/24hrs in 32 patients.

The intensity and severity of amyloid was noticed using an arbitrary grading indicated by 0 to grade 4. One-plus amyloid was found in seven cases. Two-plus amyloid was seen in 8 cases. Three-plus deposition of amyloid was

seen in 6 cases, and amyloid of Four-plus intensity was seen in 5 cases.

**Correlative Studies**

*Duration of pulmonary tuberculosis to age of onset and renal amyloidosis:*

Renal amyloidosis was present in patients with a mean duration of 4.7 years of pulmonary tuberculosis whereas the duration was shorter in patients without this lesion i.e. 3.9 years.

Table II: Relationship of age and duration to renal amyloidosis

	Renal Amyloidosis	
	Present (n=26)	Absent (12)
Mean duration of Pulmonary Tuberculosis	4.7 years	3.9 years
Mean age at the time of biopsy	44.3 years	34.09 years

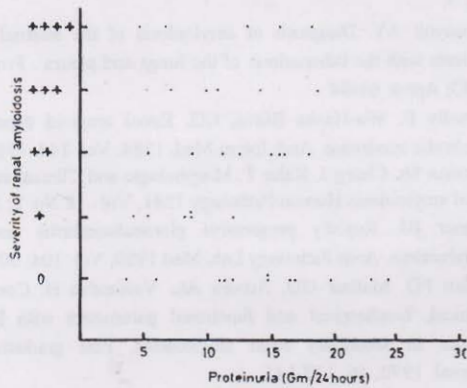


Fig 1:

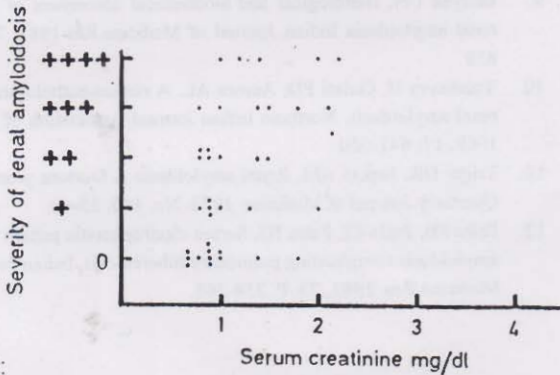


Fig. 2:

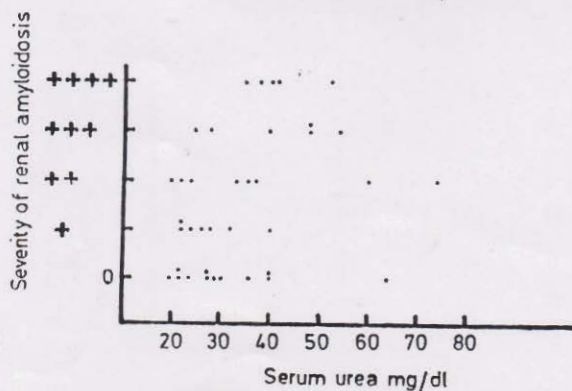


Fig 3:

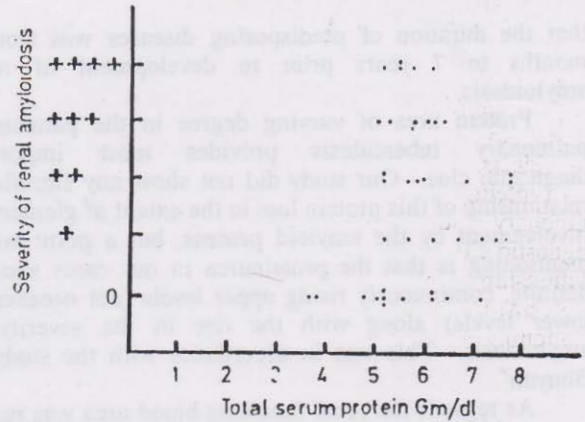


Fig.4:

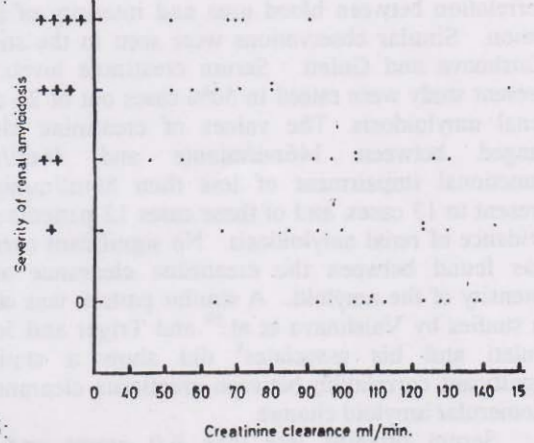


Fig 5:

Relationship of 24 hours urinary proteins to amyloidosis, of blood urea to amyloidosis, of serum creatinine to amyloidosis, of total serum proteins to amyloidosis, of creatinine clearance to amyloidosis are shown in figures 1-5

**Discussion**

Amyloidosis is a multi-system disorder, and it is the kidneys, which usually get involved and lead to serious complications or even death of the patient<sup>2</sup>. Renal failure generally corresponds to severe glomerular amyloidosis and tubular atrophy<sup>6</sup>. Common clinical manifestations of resulting nephropathies are proteinuria and nephrotic syndrome. Acute or chronic renal failure may occur and rarely abnormalities of tubular functions are seen<sup>7</sup>. The present study was undertaken to find the relationship, if any, between the biochemical and functional parameters with histological lesions in renal amyloidosis. It is well-known that amyloid deposits in the kidney provide the first and sometimes the only clue to the presence of this disorder in the body<sup>8</sup>. As regards, the range of predisposing disease that is pulmonary tuberculosis was between 2 and 12 years in our patients. The mean duration of pulmonary tuberculosis in the present series was 4.5 years in those who had renal amyloidosis and 3.9 years without it. Gulati and his associates<sup>8</sup> pointed out

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that the duration of predisposing diseases was from 5 months to 7 years prior to development of renal amyloidosis.

Protein urea of varying degree in the patients of pulmonary tuberculosis provides most important diagnostic clue. Our study did not show any significant relationship of this protein loss to the extent of glomerular involvement by the amyloid process, but a point worth mentioning is that the proteinuria in our cases showed definite, continuously rising upper levels (not necessarily lower levels) along with the rise in the severity of amyloidosis. This was in accordance with the study of Bhuyan<sup>9</sup>.

As regards the renal functions blood urea was raised over 40mg/dl in only 21% of cases. There was no obvious correlation between blood urea and intensity of amyloid lesion. Similar observations were seen in the studies of Vaishnava and Gulati. Serum creatinine levels in the present study were raised in 50% cases out of 26 cases of renal amyloidosis. The values of creatinine clearance ranged between 146ml/minute and 46ml/minute. Functional impairment of less than 80ml/minute was present in 13 cases, and of these cases 12 patients showed evidence of renal amyloidosis. No significant correlation was found between the creatinine clearance and the intensity of the amyloid. A similar pattern was observed in studies by Vaishnava et al.<sup>10</sup> and Triger and Joekes<sup>11</sup>. Gulati and his associates<sup>8</sup> did show a statistically significant correlation between creatinine clearance with glomerular amyloid change.

Serum proteins less than 6.0 grams and serum albumin of less than 3.0 grams were present in 13 cases of renal amyloidosis. Hypoproteinemia and hypoalbuminemia were present with valuable frequency in cases with renal amyloidosis. Albumin/globulin ratio was reversed, mean was 1.0 (normal is 2.46) in our series of cases. This finding was in accordance the findings of Patra et al<sup>12</sup>.

### Conclusions

Amyloid is found to be the most common cause of renal malfunction in cases of pulmonary tuberculosis. No blood test is diagnostic of amyloid. There was no correlation

found between biochemical findings and severity of renal amyloid.

### Suggestions

It is inferred from the present study that renal assessment in cases of pulmonary tuberculosis has its importance because it is likely that a patient who can be cured with anti-tubercular can drugs go into a fatal state of renal failure over a period of time.

### References

1. Philip NH. Amyloidosis in Medicine International 1994; Vol. 7, Number 25 76-82
2. Philip NH. Amyloidosis in Medicine International 1990; Vol. 3, Number 11-3338-3345
3. Kitamoto T, Tashima T and Tateishi J, Novel histochemical approaches to the Prealbumin-Related Senile and Familial forms of systemic amyloidosis. American Journal Pathology 1986 Vol. 123 No. 3.
4. Panasyuk AV. Diagnosis of amyloidosis of the internal organs in patients with the tuberculosis of the lungs and pleura. Probl Tuberk. 1983; Apr 4: 61-64
5. Conolly P, Wu-Haotu Biava, CG. Renal amyloid deposition and Nephrotic syndrome. Arch Intern Med. 1984. Vol. 144: 198
6. Dikman Sh, Churg J, Kahn T. Morphologic and Clinical correlates in renal amyloidosis Human Pathology 1981, Vol. 12 No. 2: 160-169
7. Panner BJ. Rapidly progressive glomerulonephritis and possible Amyloidosis. Arch Pathology Lab. Med 1980, Vol. 104: 603-609
8. Gulati PD, Mathur GD, Aurora AL, Vaishnava H. Correlation of Clinical, biochemical and functional parameters with histological lessons in secondary renal amyloidosis. Post graduate Medical Journal. 1970, 46: 137-141
9. Bhuyan UN, Histological and biochemical assessment of severity of renal amyloidosis Indian Journal of Medicine. Res-1981, 73. P 430-438
10. Vaishnava H, Gulati PD, Aurora AL. A clinico-pathological study of renal amyloidosis. Northern Indian Journal Association of Physicians 1969. 17: 641-650
11. Triger DR, Joekes AM, Renal amyloidosis A fourteen year follow up Quarterly Journal of Medicine: 1973. No. 165: 15-40
12. Patra SB, Jhala CI, Patra BS. Serum electrophoretic pattern amyloidosis complicating pulmonary tuberculosis. Indian Journal of Medicine Res. 1981, 73. P. 258-265.