SUMMERY AND CONCLUSION

Amyloidosis comprises a group of protein-folding disorders of diverse etiology in which normally soluble proteins are deposited as insoluble fibrils that have a characteristic, highly ordered abnormal conformation that share unique staining properties and progressively disrupts tissue structure and impairs function. leading to progressive disease. **(Pepys, 2006)**

Amyloidosis can affect different organs in different people, and there are many types of amyloid. Amyloidosis frequently affects the heart, kidneys, liver, spleen, nervous system and gastrointestinal tract **(MFMER et al, 1998-2009) .**

Amyloid protein can be deposited in a localized area or only affect a single tissue of the body. This form of amyloidosis is called localized amyloidosis. While amyloidosis that affects tissues throughout the body is referred to as systemic amyloidosis. Many amyloidoses are inherited, due to mutations in the precursor protein. Other forms are due to different diseases causing overabundant or abnormal protein production . **(Eder, Bitterman, 2007)** Out of the approximately 60 amyloid proteins that have been identified so far **(Mok et al, 2007)**

Types of amyloidosis are based on the precursor protein that form the amyloid fibrils and the distribution of its deposition **(National Institute et al,June 12, 2009)**

Determination of the Type of Amyloidosis are indistinguishable by light or electron microscopy, the most direct method is by mass spectrometry or amino acid sequencing of proteins

(Lachmann ,2004) while the most definitive method used in the clinical setting is immunofluorescence or immunohistochemical staining of tissue using antibodies that are directed against known amyloidogenic.and finaly by demonstration of a monoclonal Ig protein in the blood or urine or clonal plasma cells in the bone marrow**(Palladini et al,2006)**

Renal Amyloidosis is either the result of primary fibrillar deposits of immunoglobulin light chains [amyloid L (AL)], or secondary to fibrillar deposits of serum amyloid A (AA) protein fragments , In systemic AL amyloidosis (primary amyloidosis), light chains produced in excess by clonal plasma cell dyscrasias are made into fragments by macrophages , nephrotic syndrome is common, and about 20% of patients progress to dialysis. Also secondary amyloidosis affects the kidney with nephrotic syndrome. Glomerular involvement by amyloidosis is frequent and explains the proteinuria that these patients exhibit. Amyloidosis is often diagnosed by renal biopsy **(Teng et al,2004)**. Amyloid formation can be influenced by altering lysosomal function or the mesangial milieu, Once amyloid is produced and delivered to the extracellular mesangial matrix, activation of metalloproteinases occurs, with eventual destruction of the mesangial matrix and replacement by amyloid **(Keeling , Herrera, 2005)** Dialysis related amyloidosis is one of the most serious complicaions associated with long term hemodialysis,it may be seen occasionally in patient with long standing sever renal failure who are not treated by dialysis**(Maeda,2000)**

B2-Microglobulin is the subunit protein in the amyloid associated with long-term dialysis. This nonglycosylated, 11,800 dalton protein is normally present in most biologic fluids, including serum, urine, and synovial fluid. It is filtered by glomeruli and catabolized after proximal tubular reabsorption.Serum levels range up to 2.7 mg/L (0.23 mcmol/L) in healthy individuals. Because the rate of B2-microglobulin synthesis exceeds the rate of its removal by dialysis, serum levels are often elevated; the degree of residual renal function appears to be the most important factor in determining the extent of this elevation. When residual renal clearance is minimal, serum B2-microglobulin levels depend substantially on the type of dialysis being given; levels are then lower in patients treated with high-flux dialysis or hemodiafiltration than in those being treated with low-flux cellulose-based dialyzers.

Nonenzymatic glycation of B2-microglobulin may be important. Advanced glycation end product (AGE) modification of proteins confers resistance to proteolysis, increased affinity for collagen, and the ability to stimulate activated mononuclear leukocytes to release proinflammatory cytokines. AGE-modified proteins are poorly cleared by dialysis. AGE-modified B2-microglobulin has been identified in amyloid deposits; the propensity for B2-microglobulin amyloid to deposit in osteoarticular tissue may be due to the enhanced binding of AGE-modified proteins to collagen.

(Daugirdas et al,2007)

The clinical presentation of dialysis related amyloidosis is carpal tunnel syndrome,large and medium sized joint arthropathy which presented by arthralgia , decrease joint mobility , effusion

incapacity**(Hoffman et al,2004**) ,spondyloarthropathy which most frequently occur at the cervical spine and this may be asymptomatic or lead to mild spinal pain or may cause nerve root compression,bone cyst contain B2microglobulin amyloid deposits **(Bardin et al ,1995)** ,intestinal obstruction , spontaneous tendon rupture , renal stones composed of B2microglobulin may occur (**Harrison's, 2009) (Traut et al,2007)**.

As the diagnosis of amyloidosis requires histological demonistration of amyloid deposits , any tissue can be evaluated for congo red stain positivity , The likelihood of a missed diagnosis is lower with a kidney biopsy than with biopsies of other tissues because amyloid fibrils are visible by electron microscopy **(Balal et al ,2004)** and demonstrated by mass spectrometry or amino acid sequencing of proteins that are extracted from the amyloid deposits , Computed tomographic scan and magnetic resonance imaging scan of bone will provide additional information of bone complications**(Current et al, 2009)**

Treatment includes symptomatic treatment with steroid therapy, nonsteroidal anti-inflammatory drugs for bone pain , Endoscopic resection of coracocromial ligament for shoulder pain , Surgical therapy including joint replacement and carpal tunnel release as necessary **(Zingraff et al ,1995) (Satoskar et al, 2007)**

Also the use of high flux membrane in hemodialysis such as the polyslfone F60 or the polyacrylonitrite AN69 membrane allow to clear more or less marked amount of polypeptide **(Lonnemann, 2000)**. and to remove large molecular weight solutes including

B2microglobulin with better Biocomatibility than conventional unsubstituted cellulose **(Sanchez et al , 1993)**

While early renal transplantation is considered suitable for all patient before the development of established dialysis related amyloidosis it will rapidly normalize serum B2microglobulin level in patients who have seen on dialysis for less than 8 years **(Stangou et al,2005)**