Summary and Conclusion

Chronic kidney disease (CKD) became in the last decade an important medical and social problem worldwide. Most of these patients have cardiovascular disease (CVD), and over half of them will die due to a cardiovascular cause. The pathogenesis of cardiovascular damage in CKD patients is far more complex than in the general population, as they are exposed to a number of cardiovascular risk factors. They not only include those identified in the general population, whose prevalence is far higher among dialysis patients, but also additional risk factors specific to CKD, eventually exacerbating after the start of dialysis. Strategies to reduce cardiovascular disease in these populations have been based on the identification and modification of the risk factors.It is clear that some of these risks are modifiable and can be improved with currently available therapy.

There are several biomarkers present in the blood and body fluids of CKD patients which represent a major challenge in predicting and controlling cardiovascular disease such as BNP, cardiac Troponins, markers of chronic inflammation, oxidative stress, endothelial dysfunction, fetuin A, subclinical hypothyroidism and advanced glycation end products .Finding or measuring the level of these biomarkers may be useful for prognostication and stratification of cardiovascular risk.

BNP is avasopeptide hormones that have major role in regulating Pressure and volume through direct effects on the kidney and systemic vasculature. The main stimulus for BNP or NT-pro-BNP synthesis and secretion is increased LV wall stress. Thus, circulating BNP or NT-pro-BNP levels reflect the degree of LV overload. Numerous studies demonstrated a close association between BNP or NT-pro-BNP level and LV mass and systolic function in the ESRD population. The ability of BNP and NT-pro-BNP to predict mortality and adverse cardiovascular outcomes in the ESRD population has been examined in numerous studies.

Cardiac Troponins (T and I) are released into the circulation with myocardial injury. Thus, measuring circulating cTnT and cTnI level using high-sensitivity assays has become the gold standard approach in diagnosing acute myocardial necrosis. Levels of cardiac troponin are frequently elevated in the absence of acute coronary syndrome among patients with varying degrees of kidney disease, and cTnT is more

frequently increased compared with cTnI in asymptomatic patients with ESRD. In fact, cTnT elevation had even greater prognostic importance among patients with mild to moderate degrees of kidney disease, clearly confirming the specificity of cTnT as a marker of myocardial injury among patients with kidney disease. cTnT is more useful on a routine basis than cTnI in patients with ESRD because the frequency of elevated cTnI associated with increased risk for adverse events is markedly lower than that for cTnT.

various inflammatory biomarkers, such as C-reactive protein (CRP), IL-6, fibrinogen, pentraxin-3, S-albumin, and white blood cell count act as independent predictors of mortality in patients with CKD. Although the release of pro-inflammatory cytokines may have acute beneficial effects, chronic systemic elevation is likely to produce detrimental effects. Indeed, this is the problem faced in CKD, in which a state of persistent low-grade inflammation is commonly observed. The observation that both protein-energy wasting (PEW) and persistent inflammation are highly prevalent in patients with ESRD and are associated with a substantially increased mortality risk has generated much interest.

The vascular calcification is a major cause of increased morbidity and mortality in dialysis patients., low levels of circulating fetuin-A and Serum MGP are associated with increased cardiovascular burden and mortality. As the severity of coronary calcification increased, serum MGP levels were significantly decreased. Also Hyperhomocysteinemia may contribute to the pathogenesis of atherosclerosis by injuring the endothelium and promoting coagulation.

Endothelial dysfunction is a well-documented early phenomenon in atherosclerosis that precedes structural changes and clinical manifestations. Decreased endothelial function is thought to primarily reflect a decreased bioavailability of nitric oxide (NO). Biomarkers such as ADMA, PTX3 and circulating EPC play important roles in this process. Elevating levels of ADMA and PTX3 are believed to be a true independent indicator of disease activity and intimately linked to endothelial dysfunction. decreased numbers of circulating EPC, which may have a role in neovascularization of ischemic tissue also play the same role.

Increased levels of oxidative stress markers are present in the plasma of CKD patients, which indicates that uremia is a prooxidant state. Indeed, the elevation

of plasma F_2-isoprostane concentration has been demonstrated in CKD patients. The presence of oxidative modifications of proteins, which are also good oxidative stress plasma markers, have also been demonstrated in CKD patients. The presence of numerous defects in the antioxidant defense system, which leads to a decrease in the clearance of reactive oxygen species, can be used as indirect oxidative markers. Increased oxidized to reduced plasma ratio of vitamin C and red blood cell glutathione has been demonstrated in dialysis patients. Moreover, dialysis treatment seems ineffective in the correction of oxidative stress. Few data are available regarding the success of interventional trials with antioxidant treatment strategies aimed at reducing CVD in CKD patients such as oral vitamin E supplementation and antioxidant N-acetylcysteine.

CKD per se causes alterations in thyroid hormones in the absence of an underlying intrinsic thyroid disorder characterized by a decrease in total (T_3) and free (fT_3) triiodothyronine concentration while thyroid-stimulating hormone levels are normal. Indeed, a low T_3 level has recently been shown to be an independent predictor of all-cause mortality in prevalent HD and peritoneal dialysis patients as well as incident dialysis patients. Although the reasons for this observation are yet unknown, they may caused by the links between a state of subclinical hypothyroidism and low-grade persistent inflammation.

Early renal impairment is associated with an increase in mean lipoprotein (a) concentration. lipoprotein (a) concentrations are negatively correlated with glomerular filtration rate. Raised lipoprotein (a) concentrations are associated with an increased risk of coronary-artery disease and of other form of vascular disease.

Secondary hyperparathyroidism is often the first and most recognizable endocrinal laboratory finding in CKD patients. parathyroid hormone (PTH) is a compensatory mechanism to maintain calcium and phosphorus levels within physiological ranges despite renal phosphate retention and decreasing 1,25 dihydroxyvitamin D production. Clinical studies indicate that PTH may contribute to the development of left ventricular hypertrophy**.** Increased PTH levels can exacerbate atherosclerosis by contributing to hyperlipidemia and impaired glucose tolerance. Effects of PTH on vascular endothelial function and growth may contribute to increased vascular tone and stiffness,