INTRODUCTION AND AIM OF WORK

Hypertension is a late manifestation of a much broader syndrome of cardiovascular risk factors such as abnormalities of lipid profile, insulin resistance, changes in endocrine and renal function, obesity, left ventricular hypertrophy and diastolic dysfunction. These associated risk factors may be present for years before the onset of high blood pressure and may precipitate coronary event either before or after the onset of high blood pressure. In addition, it appears that many of the changes in vascular structure and function occur before the onset of high blood pressure and may be responsible for its ultimate development. In these patients, treatment of high blood pressure will have very little impact on the outcome. **(Neutel and Smith, 1995, Neutel, 2001and Glasser, 2001).**

The development of high blood pressure in patients with hypertension syndrome may represent an advanced or perhaps irreversible stage of the disease process, and it is possible that treatment after this stage can only control blood pressure and slows the progression to cardiovascular disease. Identification and treatment of those patients before the onset of high blood pressure may provide a better opportunity for reversing disease process and protecting them from developing cardiovascular disease (CVD) **(Neutel *et al.*, 1999 and Abarquez, 2001).**

Hyperhomocysteinaemia is increasingly recognized as risk factor for vascular disease affecting heart, brain, and extremities. A considerable

amount of genetic, biochemical, pathophysiological, clinical and epidemiological data suggest a causal role for hyperhomocysteinaemia in the development of atherosclerosis and thrombosis. Patients with sever inherited forms of hyperhomocysteinaemia are at a very high risk of cardiovascular events. Moderate hyperhomocysteinaemia is frequent in patients with CVD (**Chico *et al.*, 1998 , Durand *et al.*,2001 , Desouza *et al.*, 2002 and Boysen *et al* ., 2003).**

Endothelins (ET) are potent 21-amino-acids vasoconstrictor peptides produced in different tissues, particularly the endothelium of blood vessels. Endothelin-I plays an important role in the pathophysiology of cardiovascular and renal diseases. This is recognized by the potential therapeutic use of endothelin antagonists or endothelin converting enzyme inhibitors **(Schiffrin, 1998 , Moreau and Dao, 2001, Ramuzzi ,2002 and Schiffrin , 2003).**

Asymmetric dimethylarginine (ADMA) is an endogenous and competitive inhibitor of nitric oxide synthase. Plasma levels of this inhibitor are elevated in patients with atherosclerosis and in those with risk factors for atherosclerosis. In these patients, plasma ADMA levels are correlated with the severity of endothelial dysfunction and atherosclerosis. By inhibiting the production of nitric oxide, ADMA may impair blood flow, accelerate atherogenesis, and interfere with angiogenesis. ADMA may be a novel risk factor for vascular disease. **(Cooke , 2000 and Kielstein *et al.*, 2003).**