I N T R O D U C T I O N

INTRODUCTION

Diabetes mellitus is a common serious metabolic disorder. Its true frequency varies from 1-2% in general population. Disease is characterised by metabolic abnormalities in the form of hyperglycemia, hyperlipidemia and glycosuria.

Common complications are retinopathy, diabetic nephropathy, ischemic heart disease and atherosclerosis.

Renal disease is the commonest complication and leading cause of death in diabetes. Diabetes affects the structure and function of kidney in many ways. Diabetic nephropathy is presented with variety of clinical syndromes like mild asymptomatic proteinuria, nephrotic syndrome, hypertension and progressive renal failure.

Diabetic nephropathy represents the single most important cause of renal failure in adults in the western world, causing 25% of all new cases of uremia. The peak incidence for the development of clinical renal disease occurs after about 16 years of insulin dependent diabetes mellitus. Over all, approximately 35-45% of patients, with long standing insulin dependent diabetes mellitus will ultimately develop diabetic nephropathy, defined as dipstick positive proteinuria, hypertension and falling GFR (Christiansen and Anderson et al, 1985).

In insulin dependent diabetic patients incidence of nephropathy is 40-50% (Wetzel et al, 1986) while less

in non insulin dependent diabetes. One in four end stage renal disease patients turns out to be diabetic(Mogensen, 1984). The mortality in patients suffering from diabetic nephropathy is upto 100 times that of age and sex matched background population, and this is mainly due to enormous deaths from end stage renal disease (Borch Johnsen et al, 1985).

During the first decade of diabetes, values for urinary albumin excretion rate usually remains normal, averaging $<$10 mg/day there are, however, at least two circumstances in which transient increase in urinary albumin excretion may be observed in patients with early diabetes. First, elevation of UAE may be observed during episodes of poor metabolic control. Values for UAE in this setting usually remains $<$50 mg/day but higher values have some times been recorded.

Second, exercise may increase UAE to values as high as 500 mg/day in diabetic patients whose reading values for UAE are normal (Vittinghus and Mogensen, 1982).

Diabetic nephropathy is diagnosed by urinary excretion of protein in the range of 30-300 mg/24 hours which is called as microalbuminuria and more than 300 mg/24 hours is clinical proteinuria (Mogensen et al, 1987). In microalbuminuria cases, renal functions are normal and urine is negative for clinical proteinuria (Vibreti et al, 1979).

Diabetic nephropathy progression leads to glomerulosclerosis which causes decreased nephron population along with increase in single nephron GFR and leads to solute over load of that single nephron causing damage to endothelium, mesothelium, epithelium, ultimately frank proteinuria and renal failure.

Diabetic nephropathy is classified in 5 stages of Mogensen et al (1976).

Stage I : Early renal hypertrophy and hyperfunction.

Stage II : Renal lesion without clinical signs.

Stage III : Incipient diabetic nephropathy.

Stage IV : Clinical overt.

Stage V : End stage renal failure.

The observations that proteinuria precedes loss of renal function in diabetic patients has led naturally to the assumption that maneuvers which reduce proteinuria will also retard the progression of diabetic renal disease. Morphometric studies suggest that the reduction of GFR in diabetic nephrology is caused by progressive expansion of the glomerular mesangium. It is not certain that all maneuvers which reduce proteinuria will prevent reduction of the GFR in diabetic patient.

Microalbuminuria is now considered to be a marker of earlier renal disease in IDDM patients and an indicator of susceptibility to cardiovascular complications.

Several therapeutic interventions, such as glycemic control, antihypertensive treatment and low to moderate protein diets have been shown to be effective in reducing microalbuminuria (Brouhard and Lagrone, 1990; Ciavarella et al, 1987; Evanoff et al, 1987; Kupin et al, 1987; Rudberg et al, 1988 and Zeller et al, 1991).

The management of diabetic patients with advanced nephropathy is not easy, because such patients tends to have the nephrotic syndrome and severe damage of many other organs, consequently, it would be of great value to try and alleviate the massive proteinuria which is characteristic of this condition. In early stages of diabetic nephropathy, several maneuvers and drugs have been tried to reduce the proteinuria and retardation of progression of nephropathy. Now-a-days ACE inhibitors are much in use specially captopril for the reduction of proteinuria and improvement of renal function in diabetic nephropathy cases.

Recently lisinopril which is being argued as a better ACE inhibitor as compared to captopril in the management of hypertension, has been utilized in diabetic nephropathy cases. One to the paucity of literature about the use of lisinopril in diabetic nephropathy with or without hypertension, thus study has been designed to know the effect of captopril versus lisinopril in cases of diabetic nephropathy.
