Summary

Stroke is a serious ailment because it is the third leading cause of death, after heart disease and cancer. In 2003, it accounted for approximately one of every 15 deaths, or a total of 273,000 deaths. This translates to one stroke death every 2 minutes. For the year 2003, the American Heart Association estimated 700,000 new strokes (200,000 of which were recurrent).

So, on average, in the United States, someone had a stroke every 45 seconds. Studies have reported a 3 to 9% greater risk for hospitalization for symptomatic stroke in dialysis patients relative to the general population, making stroke awareness critical in the nephrology community.

Cerebrovascular disease includes both Transient Ischemic Attacks (TIA) and stroke. Stroke is commonly defined as the sudden onset of focal neurologic or retinal symptoms associated with cerebral or retinal tissue ischemia. The focal symptoms can include hemiparesis, hemiparesthesia, aphasia, visual field cuts, monocular blindness, diplopia, dysarthria, and imbalance.

TIA has been defined as neurologic symptoms caused by ischemia, which resolve within 24 hours. This definition, however, has been undergoing revision. The new proposed definition is the presence of neurologic symptoms for < one hour with the absence of any radiologic changes on Magnetic Resonance Imaging (MRI) that correlate geographically with the symptoms; diffusion-weighted images are most sensitive for cerebral ischemia.

Vascular occlusion in the cerebral circulation results in ischemia of cerebral tissue that causes tissue infarction. Approximately 80% of strokes are ischemic. In between 10 and 20% of strokes, the infracted tissue subsequently hemorrhages.

Patients with ESRD are characterized by an increase in age-adjusted mortality of between 10 and 50 times and a reduction in remaining life expectancy from one-sixth to one-third of the general population.

Cerebrovascular disease is a common cause of death in chronic dialysis patients. Clinically overt vascular disease is prevalent at the initiation of dialysis, when up to 30% of patients have evidence of coronary artery disease, 20% have peripheral vascular disease and 20% have cerebrovasuclar disease.

Several cohort studies have demonstrated a similar prevalence of clinically overt vascular disease in moderate CKD and ESRD. In a group of 186 patients with moderate to severe CKD with a mean GFR of 31.8 ± 16.2 ml/minute and age of 68.1 ± 14.1 years, a 27% prevalence of coronary heart disease, 22% prevalence of cerebrovascular disease and 23% prevalence of peripheral vascular diseased has been demonstrated with no significant differences in the prevalence of disease in these territories to that reported in age-matched patients at the commencement of dialysis.

The incidence of hospitalized stroke in dialysis patients is increased at least four times compared to the general population. These vascular events significantly reduce patient survival, result in

the 'non-traditional' risk factors which arise due to the metabolic abnormalities associated with reduced renal function (high calcium-phosphate product, homocysteinaemia and oxidative stress). A strong association between protein-calorie Malnutrition, systemic Inflammation and Atherosclerosis (MIA) syndrome has been described in ESRD.

There is a high prevalence of traditional vascular risk factors such as hypertension, dyslipidaemia and diabetes in patients at the initiation of dialysis. Traditional vascular risk factors are also evident in patients with CKD. In a cohort of patients with moderate to severe CKD, the majority of patients had one or more modifiable vascular risk factor with hypertension being present in 89%, dyslipidaemia in 68%, diabetes in 32% and current smoking in 7% of subjects.

There is now compelling evidence that vascular disease is a feature of early CKD, numerous, interrelated factors have been identified, which may contribute to vascular risk in patients with renal disease. At present, the relative importance of these potential risk factors in contributing to overall vascular risk in CKD is not known. It is possible that the risk profile of patients with renal disease changes as GFR decreases, or, that different CKD patients have different vascular risk profiles. In early CKD, hypertension is a major risk factor which may also contribute to some of the functional and structural changes observed in patients with more advanced CKD. IR may be an early feature of renal disease, which becomes more severe as renal function declines, and which may

account for the propensity of CKD patients to develop multiple vascular risk factors. Falling GFR is also associated with altered calcium phosphate homeostasis, homocysteinaemia and increasing ADMA levels, which further compound total vascular risk. In some patients, the added effects of chronic inflammation manifest as both malnutrition and vascular disease. Thus, while increased vascular risk exists from the earliest stages of renal disease, it is likely that vascular risk compounds as residual renal function declines. Most large studies examining the effects of risk factor intervention on vascular outcomes have excluded patients with significant renal impairment. There remains an urgent need for large randomized clinical trials investigating the effect of risk factor modification on vascular outcomes in CKD.