Chapter 3

Aims and Objectives
3. Aim

Chronic renal failure is a worldwide public health problem with significant comorbidity and mortality. Improving the quality of life and survival of CRF patients necessitates a large number of preventive and therapeutic interventions. Oxidative stress is purported to play an important role in the pathogenesis of chronic renal failure. Even though the presence of oxidative stress in chronic renal failure has been well established, the consequences of oxidative stress in this pathological condition have not been well elucidated. This knowledge will provide an opportunity to assess the benefit of antioxidant therapy in retarding or preventing the progression of renal dysfunction in chronic renal failure patients. Accordingly, the objectives of this thesis were:

- To investigate oxidative stress markers in patients with CRF, comparable healthy controls and to characterize their relationship to renal function and to evaluate the protective effects of antioxidants on renal function in animal models.

- To delineate the possible role of oxidative stress on insulin resistance per se in vivo and to determine if insulin resistance is associated with oxidative stress in CRF.

- To explore if oxidative stress and antioxidants could modulate the genesis of early glycated proteins and to examine the possible role of oxidative stress in increased glycated protein levels in CRF.

- To examine the relationship between markers of oxidative stress and conventional risk markers of cardiovascular risk factors in patients with CRF and to evaluate the possible protective role of antioxidants in animal model.
Specific Objectives

The specific aims of clinical and experimental studies were:

Human Study

1. To check for the oxidant and antioxidant status in plasma and erythrocyte in patients with chronic renal failure.
2. To study the possible alteration in insulin resistance in non-diabetic undialyzed chronic renal failure patients.
3. To examine the possible changes in inflammatory markers in these patients.
4. To study the non-enzymatic glycation by assay of fructosamine and glycated hemoglobin in patients with chronic renal failure.
5. To study, based on the data obtained, the relationship of oxidative stress with glycation, insulin resistance and inflammatory status perturbation in undialyzed, non-diabetic CRF patients.

Animal Study

1. **Experimental rat model of chronic renal failure**

   1. To check for the oxidant and antioxidant status in plasma and erythrocyte of CRF rats.
   2. To study the possible alteration in glucose tolerance of CRF rats.
   3. To examine the lipid profile patterns in CRF rats.
   4. To study the effect of adenine and antioxidant supplementation on redox sensitive serine kinase pathways in rats – NF-kB, JNK and p38MAPK.
   5. To study the effect of adenine on proximal insulin signaling pathway in rats.
   6. To examine the possible beneficial effects of taurine and green tea on the above mentioned alterations in CRF rats.
2. Experimental rat model of oxidative stress

1. To check for the oxidant and antioxidant status in plasma and erythrocyte of rats subjected to oxidative stress.

2. To study the possible alteration in glucose tolerance in these rats.

3. To study the effect of oxidative stress per se on redox sensitive serine kinase pathways – NF-kB, JNK and p38MAPK.

4. To study the effect of MnCl₂ on proximal insulin signaling pathway.

5. To examine the possible beneficial effects of taurine and green tea on the above mentioned alterations in CRF rats.

3. Experimental rabbit model of oxidative stress

1. To check for the oxidant and antioxidant status in plasma and erythrocyte of rabbits subjected to oxidative stress.

2. To study the possible alteration in glucose tolerance in these rabbits.

In vitro study

1. To investigate the role of hydrogen peroxide per se on glycation of hemoglobin.

2. To explore the possible role of malondialdehyde per se on glycation of hemoglobin.

3. To explore the influence of reduced glutathione per se on the process of protein glycation.

4. To explore the protective role of taurine on glycation of hemoglobin and lipid peroxidation in erythrocytes exposed to pathological concentration of glucose.

5. To study the possible beneficial effect of green tea on reducing the processes of protein glycation and lipid peroxidation.