# INTRODUCTION AND AIM OF THE WORK

## RENAL REPLACEMENT THERAPY

Before 1970, therapeutic options for patients with kidney failure were quite limited. Only a small number of patients received regular dialysis because few dialysis facilities had been established. Patients underwent extensive medical screening to determine their eligibility for ongoing therapy, and treatment was offered only to patients who had renal failure as the predominant clinical management issue. Patients with other systemic illnesses apart from kidney failure were not considered for chronic dialysis therapy. Kidney transplantation was in the early stages of development as a viable therapeutic option. Transplant immunology and immunosuppressive therapy were in their infancy, and for most patients, a diagnosis of chronic renal failure was a death sentence.

In the decade that followed, the availability of care for patients with kidney failure grew rapidly throughout the medically developed world. In the United States, the passage of Medicare entitlement legislation, in 1972, to pay for maintenance dialysis and renal transplantation, provided the major stimulus for this expansion. This trend continues unabated, at least for hemodialysis.

Despite numerous medical and technical advances, patients with kidney failure who are treated with dialysis often remain unwell. Constitutional symptoms of fatigue and malaise persist despite better management of anemia with erythropoietin. Progressive cardiovascular disease (CVD), peripheral and autonomic neuropathy, bone disease, and sexual dysfunction are common, even in patients who are judged, using established, objective criteria, to be treated adequately with dialysis because the most efficient hemodialysis regimens currently provide only 10% to 12% of the small-solute removal of two normally functioning kidneys. Removal of higher-molecular-weight solutes is even less efficient.

For most patients with kidney failure, kidney transplantation has the greatest potential for restoring a healthy, productive life ***(Demonicio et al., 2007)***. However kidney transplant recipient shouldn't expect himself away from complications of chronic kidney disease (chronic allograft nephropathy), also practitioners of kidney transplantation must consider the accepted rate of graft loss weather early graft loss or late graft loss.

Grafts can be lost early due to immunologic and non immunologic causes, immunologic causes include accelerated acute rejection,early cell mediated rejection and antibody mediated rejection while non immunologic causes include technical vascular complications (graft artery or graft vein thrombosis), urologic complications(urinary leak) and thrombotic microangiopathy).

Late graft loss which is the main topic of this essay is defined by loss of the graft 1 year after kidney transplantation. It is also caused by immunologic and non immunologic causes. For example, death with functioning graft (DWF) which accounts for 50% of late graft loss is caused by either cardiovascular complications (non immunologic causes) or infections and malignancy (immunologic causes as a state of over immunosuppression).

Causes of late graft loss will be discussed in the next pages

## DEFINITION OF LATE GRAFT LOSS

By the term (late graft loss), most authors mean the loss of renal allograft 12 months after kidney transplantation ***(Kandaswamy R et al., 2007).***

## CAUSES OF LATE GRAFT LOSS

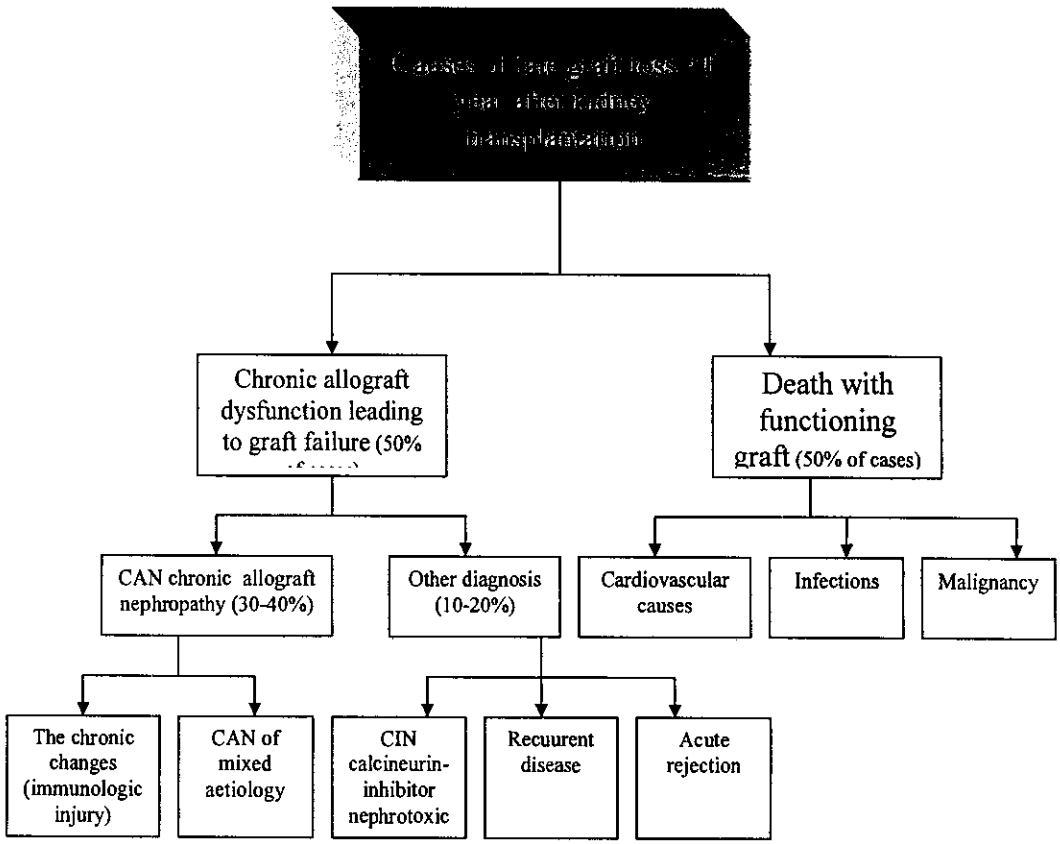
Grafts can be lost due patient death with functioning graft (DWF) or graft failure ***(Kandaswamy R et al., 2007).*** Among causes of graft failure; two major causes , development of chronic allograft nephropathy ***(Lut ZJ et al., 2007)*** and recurrence of glomerulonephritis, also discontinuation of immunosuppressive medication by non compliant patients plays a great role in late graft loss ***(Hocker B et al., 2006).***

Many factors co-existing during dialysis will impact graft survival, for example Pre-transplant hypertension which participate in development of chronic allograft nephropathy. Chronic allograft nephropathy can be caused by alloantigen-dependant factors ***(Tullius et al., 1995)*** like HLA mismatch, prior sensitization,episodes of rejection, drug non compliance and Suboptimal immunosuppression, also it can be caused by alloantigen-independent Risk factors ***(Tullius et al., 1995)*** including hypertension,calcineurin inhibitors nephrotoxicity, infections and hyperlipidemia , etc...

Although kidney transplantation confers the highest survival benefit among different renal replacement therapies, renal allograft recipient still have a high mortality rate compared with age-matched population controls ***(Arsend et al., 1997).***

It has been reported that mortality of renal transplant recipients was 14 times higher than the age- matched. Population during the first year after transplantation and 4 times higher after this period the relatively higher mortality in renal transplant recipient due to co-morbid medical conditions.

**Figure (1): Causes of late graft loss**

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pretransplant dialysis treatment and factors uniquely related to transplantation including immunosupression and other drug effects ***(Arrazola et al., 2000).***

Death with functioning graft (DWF) which is a major cause of graft loss is caused by cardiovascular complications,infections and malignancy following kidney transplantation ***(Briggs et al., 2001).***

Despite significant improvements in one year kidney allograft survival ***(Hariharan et al., 2000),*** the rate of chronic graft loss after the first year remains substantial and may not have improved over the last decade. As an example, a study that analyzed first renal transplants performed between 1995 and 2000 found that, despite a reduction in acute rejection rates, there was no improvement over the last 10 years in long-term allograft survival ***(Miere-Kriesche et al., 2004).***

Despite this, the rate of decline in kidney allograft function appears to have slowed ***(Kasiske et al., 2005)*** suggesting that improved results relating to long-term allograft survival are possible.

**AIM OF THE WORK**

In the next pages, we will discuss late graft loss, identify risk factors, discuss causes, and put a preventive plan to avoid late graft loss (or to delay it as possible), remembering that prevention is better than cure.