Introduction

Chronic kidney disease (CKD) is a worldwide public health problem. In the United States (US), there is a rising incidence and prevalence of kidney failure **(K/DOQI guidelines, 2002)**.

The number of patients enrolled in the end-stage renal disease (ESRD) Medicare-funded program has increased from approximately 10,000 beneficiaries in 1973 to 86,354 in 1983, and to 452,957 as of December 31, 2003. In 2003 alone, 100,499 patients entered the US ESRD program **(USRDS, 2004)**.

The rising prevalence of treated ESRD can be attributed primarily to the increase in the number of patients who start renal replacement therapy (RRT) each year, and to a smaller extent, increased survival of patients with ESRD (**Hsu et al., 2004).**

Patients with ESRD consume a disproportionate share of health care resources. The total cost of the ESRD program in the US was $27 billion in 2003, a11.5 percent increase from2002 **(USRDS, 2004).**

The projected number of ESRD patients by the year 2010 has been estimated to be 661,330 and the total Medicare ESRD program cost in excess of $28 billion USD **(USRDS, 2007)**.

Renal replacement therapy is a term used to encompass life-supporting treatments for renal failure.

It includes:

- Hemodialysis.
- Peritoneal dialysis.
- Hemofiltration.
- Renal transplantation.

The first three treatment modalities do not cure chronic kidney disease; they are palliative treatments **(USRDS, 2007)**.

Despite the magnitude of the resources committed to the treatment of ESRD and the substantial improvements in the quality of dialysis therapy, these patients continue to experience significant mortality and morbidity, and a reduced quality of life. In 2006 alone, 82,342 ESRD patients died **(USRDS 2007)**.

Survival probabilities for dialysis patients at 1, 2, 5 and 10 years were 80, 67, 40, and 19 percent, respectively **(Obrador et al., 2002).**

Moreover, 50 percent of dialysis patients have three or more comorbid conditions, the mean number of hospital days per year is approximately 14 per patient, and self-reported quality of life is far lower in dialysis patients than in the general population **(Obrador et al., 2002) and (Winkelmayer et al., 2005).**

Renal transplantation either from living or deceased donors provides a suitable solution for these comorbidities **(Ramanathan et al, 2001).**

Trasplantation background:

Early transplantation attempts in humans, which began with transplantation of renal allografts in 1936, generally did not succeed until the discovery of immunogenetics and the implementation of immunosuppressive drugs **(Sade, 2005).**

Research on humans led to the discovery that genetic control of the HLA (The genes responsible for immunologic reactions leading to graft rejection) resides on chromosome 6 in a supergene region known as the MHC. Class I MHC antigens include HLA-A, HLA-B, and HLA-C. Furthermore, the class II MHC antigens important in transplantation are governed by *HLA-DR*, *HLA-DP*, and *HLA-DQ*.

These regions on chromosome 6 are tightly linked and constitute a haplotype **(Stefoni et al., 2004).**

Immunosuppression milestones:

Initial attempts at controlling rejection began with experiments involving total body irradiation in 1958 with poor outcome in kidney transplantation **(Richet, 1997).**

Further efforts to avoid and control rejection of transplanted organs led to the investigations of medications. In 1961, 6-mercaptopurine was prescribed for the first time to a human kidney transplant recipient. The patient unfortunately died from drug toxicity **(Schnuelle et al., 1998)**.

Roy Calne at the Peter Bent Brigham Hospital experimented with 6-mercaptopurine and its close relative azathioprine, after he had disappointing experience with total body irradiation **(Suthanthiran and Strom, 1994).**

Prednisone, a cortisone derivative, was used subsequently in cadaveric kidney transplant recipients. In 1964, it was noted that prednisone not only was useful in preventing graft failure in regular doses, but it was useful also for reversing renal allograft rejection in larger doses. However, continued use of corticosteroids permanently alters normal immune function and produces other very serious adverse effects **(Suthanthiran and Strom, 1994).**

In 1972, Swiss biochemist discovered cyclosporine in natural fungal byproducts. Cyclosporine improved graft rejection in animals by inhibiting T-lymphocyte activity **(Starzl, 2001).**

The cocktail approach, which combines cyclosporine with steroids and azathioprine, was found to be the most effective approach to immunosuppression for organ transplantation patients over the next 10-15 years **(Murray, 2005).**

More recently, this combination has been replaced by regimens that include newer immunosuppressive agents. Tacrolimus has almost completely replaced cyclosporine in liver and pancreas transplantation, and it is used in 50% or more of kidney recipients around the world. Mycophenolate mofetil has largely replaced azathioprine in most organ transplantation procedures **(Sade, 2005)..**

Additional new immunosuppressive agents that have been approved include sirolimus, FK778 and FTY720. Antithymocyte globulin (Thymoglobulin), daclizumab, and basiliximab, are currently used for induction therapy **(Kahan , 2003).**

A number of new regimens are being explored that attempt steroid withdrawal or avoidance, or calcineurin inhibitor withdrawal or avoidance **(Sade, 2005).**

Advantage of renal transplantation over dialysis:

Kidney transplantation is the treatment of choice for end-stage renal disease**.** For the following reasons **(Sade, 2005):**

1. The transplanted kidney works like the native one. So; it secretes erythropoietin and activates vitamin D.
2. The patient is not linked with a machine. So, he can work and travel freely.
3. A successful kidney transplant improves the quality of life and reduces the mortality risk for most patients, when compared with maintenance dialysis.
4. Reduce toxic effect of uremia in different body organs

Graft survival:

At present, the 1-year patient survival rate for living donors and cadaveric transplants is 98% and 95% respectively. The graft half-life for living donors and cadaveric donors is approximately 20 years and 12 years respectively (**USRDS, 2007).**

Based on more than 1200 living donor transplants performed at the Urology & Nephrology Center at Mansoura University between 1976-1998, **Ghoneim and coworkers**, **2001** reported:

1. The overall graft survival rate was 75.8% and 51.9% at 5 and 10 years, respectively, with a projected half-life of 10.7 years.

2. Three factors acted as independent variables that significantly influenced graft survival:

- The number of HLA mismatches,
- The number of acute rejection episodes
- The presence of posttransplant hypertension.