

Renal Replacement Therapy in Iran

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Dialysis and kidney transplantation are the only treatment options available for patients suffering from end-stage renal disease (ESRD). More than 1 million patients are on renal replacement therapy (RRT) worldwide, and it is forecasted that their population will be doubled within the next decade. There is a clear direct relationship between a nation's gross national product and the availability of RRT. Approximately, 90% of patients with ESRD come from developed nations.⁽¹⁻³⁾ Conversely, for the vast majority of patients who live in developing countries (roughly 85%), dialysis and transplantation are unaffordable.⁽⁴⁾ Generally, a series of influencing factors dictate the gross diversity in making decisions about the rates and modalities of the RRT. There are different reported incidences of ESRD in different countries, on the one hand, and significant variations in the culture, socioeconomic status, dialysis costs and quality, reimbursement structures, and discrepancy between the demand and supply of organs for transplantation, on the other hand.

To facilitate effective future planning by healthcare authorities, reliable and up-to-date information on the number of patients with ESRD, development trends, treatment modalities, and treatment outcomes are indispensable. Worldwide, many national and

international renal registries provide demographic and epidemiologic information on patients with kidney failure. The United States Renal Data System, the Japanese Renal Registry, and the European Renal Association/ European Dialysis and Transplant Association Registry are the most famous ones. Such databases provide a valuable basis for comparisons between the specified patient populations and aid understanding of treatment practices, policies, and the implications for the well-being of patients who undergo treatment for ESRD. Meanwhile, such information regarding ESRD incidence and different modalities of treatments are not available from large parts of developing world.^(2,5,6)

In Iran, there is a central registry system and the data of RRT centers of the country are updated every 3 months in the Management Center for Transplantation and Special Diseases (MCTSD), affiliated to the Ministry of Health (MOH). This article reviews the status of ESRD and RRT in Iran with emphasis on its incidence, prevalence, and treatment.

Although the total health expenditure is 6% of the gross domestic product (GDP) and the GDP per capita is US\$ 8900 (2006 statistics),⁽⁷⁾ different modalities of RRT are free of charge and accessible for all in Iran. A fixed reimbursement rate for dialysis and

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transplantation in both public and private hospitals is paid by the government. According to our database at the MCTSD, the number of ESRD patients on RRT in Iran, with the population of 70 million, reached about 25 000 in 2006 and regarding the increasing trend of 12% per year, it will be around 40 000 by the next 5 years. The prevalence and incidence of ESRD are 357 per million population (pmp) and 66 pmp, respectively. Currently, 48.5% of the patients are on hemodialysis, 48.5% have received transplantation, and 3% are on peritoneal dialysis.

Although there are several governmental and private organizations engaged in ESRD issue, the MOH is the main sponsor of this program through the MCTSD. This organization is responsible for not only supporting the provision of the products and services needed for patients with ESRD, but also policy making and strategic planning to implement effective mechanisms for activities that will lead to improvement of the health status of patients and to establish higher standards of treatment.⁽⁸⁾

TRANSPLANTATION

In Iran, the first kidney transplantation was performed in 1968, but until 1988, transplantation program severely lagged in growth in comparison with dialysis. Between 1980 and 1985, more than 400 patients traveled abroad to receive a kidney transplant. In 1985, the high expense of transplantation in other countries and the increasing number of patients who were on the kidney transplant waiting list urged the health authorities to establish transplant facilities inside the country. Consequently, a total of 274 kidney transplantations from living related donors were performed between 1985 and 1987.

The large number of patients with ESRD with no living related donor and unestablished cadaveric donor procurement program led to adoption of a government-funded, -regulated, and -compensated living unrelated donor kidney transplantation program in 1997. Currently, Iran has the largest reported experience of living unrelated donor transplants.⁽⁹⁻¹³⁾ As a result, the number of transplant teams increased. At present, there are 25 kidney transplantation centers nationwide, and by the end of 2006, a total of 21 359 kidney transplantations have been performed in Iran. Kidney transplant activity in

Iran reached a record of 23 transplants per million per year in 2006. Graft survivals at 1 year and 2 years are 89.1% and 87.7%, respectively. It should be mentioned that workups for the potential donor and the recipient are very similar in different transplant centers.⁽¹⁰⁾ The annual rate of kidney transplantation is between 1800 and 1900 with 75%, 12%, and 13% from living unrelated, living related, and cadaveric donors, respectively. Brain-death organ donors are 1.8 pmp, nonheart-beating tissue donors are 26 pmp, and living donors are 23 pmp. According to our registration at the MCTSD, the male-female ratio in 21 359 kidney transplants was 1.6:1. The trend of that ratio has not shown any significant changes during the previous 5 years.

All of the kidney transplant teams belong to university hospitals. To prevent transplant tourism, foreigners are not allowed to undergo transplantation from Iranian living unrelated donors. Also, they are not permitted to volunteer as kidney donors to Iranian patients. The donor and the recipient should be from the same nationality, and authorization for such transplantation should be obtained from the MCTSD.⁽¹⁰⁾ In 1997, governmental rewarding donation was legislated, and now, the living unrelated donor receives an award and 1-year health insurance following transplantation. The majority of living unrelated donors also receive compensation from recipient (overseen by the Kidney Foundation of Iran, a charity involved in this process). The results of living unrelated donor kidney transplantation in long-term follow-up with a large number of cases show that this approach (Iranian model) is as good as living related donor kidney transplantation. The organ shortage can be alleviated by using living unrelated donor kidney transplantation.^(9,12-15)

After legislation for cadaveric transplantation in 2000, a virtual network was developed. The numbers of Organ Procurement Units and Brain Death Identification Units are 13 and 18, respectively, in Iran with 30 provinces and an area of 1.648 million km². Each case of brain death is determined by 5 physicians at the university hospitals and 1 of them is specialist in forensic medicine. Physicians in charge of brain death determination are appointed by the Minister of Health. The steps taken for cadaveric kidney donation system in Iran is similar to that of many other countries.⁽⁸⁾ It should also be mentioned

that cadaveric transplantation is purely altruistic and there is no gift to families except for funeral expenses in few cases.

There are national formularies for immunosuppressive drugs. Before 1996, the available immunosuppressive drugs for maintenance therapy consisted of cyclosporine (Neoral), generic azathioprine, and prednisone. Since 2000, mycophenolate mofetil has been used instead of azathioprine and now over 95% of patients are on Cellcept. Induction therapy is carried out with antithymocyte globulin, and in some cases, with interleukin-2 receptor antibodies. The government subsidizes the essential immunosuppressive drugs (cyclosporine, mycophenolate mofetil) and provides them for all transplant recipients in a much reduced price. All patients with ESRD including kidney transplant recipients belong to a group of patients called “patients with special diseases” that are eligible for a government-provided health insurance.

HEMODIALYSIS

There was an increasing incidence of ESRD from 49.9 pmp in 2000 to 64 pmp in 2006.⁽¹³⁾ The increase in the number of admitted patients to RRT was mirrored by an increase in the number of dialysis centres (227 in 2000 to 316 in 2006) and dialysis machines, transplantation centres, and preemptive transplantation (Figure 1). The mean age of the patients on dialysis is 52.8 years (in contrast with that in transplant recipients which is 38.0 years) and male-female ratio is 1.3:1, which have not shown significant changes during this period. The advocated policy for

younger patients is *transplantation as soon as possible*.⁽¹⁶⁾ The number of preemptive transplantations increased from 328 in 2001 to 491 in 2006.

The average cost of dialysis (without the human resource and maintenance drugs expenditures) is US\$ 43.2 per treatment session that is covered by the government. In 2001, less than 5% to 10% of dialysis sessions were performed using bicarbonate-containing dialysis solution. By 2006, the target of 63% of dialysis sessions with bicarbonate-containing dialysis solution all over the country was achieved. The potassium concentration of dialysate can be varied, but 2.0 mmol/L is the usually accepted concentration. Depending on the quality of the water source, water for the dialysate is ultimately purified by reverse osmosis in all centres. Two types of biocompatible dialyzers (hemophan and polysulfone) were in use in 2005, but by the end of 2006, polysulfone replaced hemophan entirely. Reprocessing of hemodialyzers for reuse is not practiced in Iran.⁽¹⁶⁾ According to the regulations, dialysis membranes must be disposable. Since obtaining and maintaining adequate access to the circulation remains a major impediment to the long-term success of hemodialysis, arteriovenous fistula is the advocated formulary of the country due to its being the most durable and cheapest option; 61% of patients were treated with the standard thrice-weekly regimen and its trend in the last 5 years is shown in Figure 2.

Regarding anemia management, the type of intravenous iron preparation provided for patients differs substantially by country; ferric hydroxide

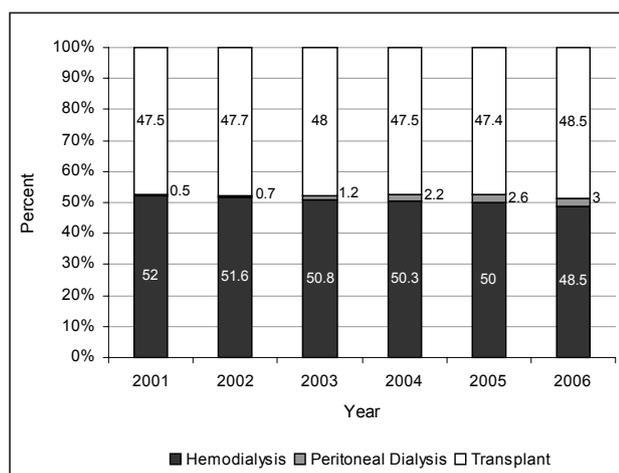


Figure 1. Renal Replacement Therapy Trend in Iran Between 2001 and 2006

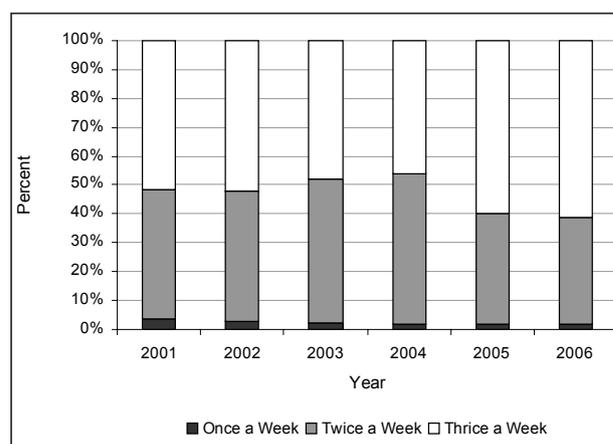


Figure 2. Weekly Dialysis Sessions in Iran Between 2001 and 2006

polymaltose (Maltofer) served as the only intravenous iron preparation used in France, while ferric or ferrous gluconate comprises more than 80% of the intravenous iron used in Germany, Italy, and Spain. Iron sucrose (Venofer) accounts for more than 93% of the intravenous iron used in the United Kingdom.⁽¹⁷⁾ In Iran, we use Venofer in all cases.

Ferritin was the most commonly performed measure of iron status of patients on hemodialysis in Iran (76.7%), similar to the reports from France, Italy, Spain, and the United Kingdom (90%), and in contrast to that in Germany (63%).⁽¹⁷⁾

PERITONEAL DIALYSIS

Continuous ambulatory peritoneal dialysis (CAPD) has come a long way since its introduction 25 years earlier. It has become a viable alternative of RRT in many developing countries.⁽⁴⁾ Continuous ambulatory peritoneal dialysis was started as pilot in 1997 in Iran. The number of patients on peritoneal dialysis (PD) is increasing, but very slowly. The conventional single-bag system, once the predominant CAPD system, has been replaced by the disconnect system. Swanneck catheters, with a resulting increase in the cost of PD are used. To reduce the costs, local production of the dialysis solution was started. Although the annual cost of CAPD is not greater than that for hemodialysis, it is not supported by public insurance agencies yet. The government provides the fund for treating dialysis patients.

Overall, this situation may reflect the fact that the dialysis facilities and the physicians receive a higher payment for hemodialysis than for PD as it has been well established. The tendency to biphasic distribution of PD utilization rate has also been previously noted.⁽⁴⁾ The disparity in PD utilization across developing countries is often inextricably linked to the local government and insurance reimbursement policies. It seems that lack of incentive to prescribe PD like that in many other developing countries with unequal reimbursement for PD and hemodialysis is a possible barrier for its publicity which needs more attention.

CONCLUSION

As a developing country, the achieved standard of RRT in Iran is acceptable, and in some aspects,

comparable with the Western countries, but the number of ESRD patients is increasing in line with global trends. Increases in hemodialysis centers, machines, and shifts, and increase in peritoneal dialysis coverage and kidney transplantation rate are being practiced, but these cannot keep pace with the increase in the number of patients. It is highly recommended that we should try to increase PD coverage and cadaveric transplantation with regard to the fact that the prevalent population of individuals with chronic kidney disease (CKD) is estimated to be at least 20 times larger than that the ESRD population.^(18,19) If no intervention is made, these people will experience progression to ESRD and need one of the RRT modalities. In the current year, provision of hemodialysis sessions for patients costs US\$ 77.4 million for the country.

Moreover, the most important adverse outcomes of CKD include not only complications of decreased glomerular filtration rate and progression to kidney failure, but also increased risk of cardiovascular diseases. Decision makers in public health and biomedical sciences should view CKD differently.⁽¹⁹⁻²⁰⁾ We can focus initially on strategies and treatments that slow progression of CKD.

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