

The Challenge of the Best Therapeutic Modality for Renal Replacement Therapy

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Introduction

Before 1970, there were few therapeutic options for people with end-stage renal disease (ESRD), and only a tiny percentage of people received regular dialysis because there weren't many dialysis centres. Patients had to be assessed to see if they qualified for maintenance medication, and only those who had renal failure as their primary clinical symptom were given treatment. The preferred therapeutic strategy of kidney transplantation was still in its infancy, and the majority of patients believed that a diagnosis of chronic renal failure meant they would soon pass away.

Fortunately, care for patients with renal failure has spread quickly throughout developing nations in recent decades. For instance, the ESRD population in Iran consists of 32,686 patients, of whom roughly half (49%) have undergone kidney transplants. The remaining population has received dialysis treatment (48% hemodialysis and 3% peritoneal dialysis) compared to 91% of the incident U.S. ESRD population, which was treated with hemodialysis, 7% by peritoneal dialysis, and 2% by preemptive transplantation [1,2].

Since 2001, the kidney transplant population has had the fastest growth, increasing by 5-6% year; however, in 2008, this growth dropped to 4.4%. In 2007, there were 2,641 patients who underwent a kidney transplant as their initial form of renal replacement therapy; in 2008, that number dropped to 2,644 [2]. Patients with renal insufficiency receiving dialysis frequently continue to be ill despite considerable medical and technological improvements. Renal transplantation gives the best chance of regaining a healthy, active life for the majority of renal failure patients. The negative effects of chronic kidney disease (CKD), which can affect candidates for renal transplantation generally, have been experienced by all transplant patients.

ESRD Incidence and Prevalence

According to reports, there were almost 2 million dialysis patients globally in 2010 [2]. Japan has the greatest prevalence rate for ESRD at 2045 per million people, followed by the United States at 1509 per million [3,4]. These high figures are a result of

policies in these two countries that give people with ESRD open access to chronic dialysis therapy and almost universal access to healthcare. The prevalence of ESRD varies widely around the globe, with certain nations reporting rates of less than 10 per million people. Only four nations-the United States, Japan, Germany, and Brazil-represent 11% of the world's population, yet they are home to 52% of the world's dialysis patients [3]. The prevalence of ESRD varies greatly between nations as well as within regions of the same nation. The wide variances in reported ESRD prevalence are likely caused by the disparities in access to care, the availability of particular therapeutic modalities, and methods of payment used across different countries.

The classification of the underlying cause of renal failure, differences in the definition of ESRD, and variations in the accuracy of the reported data should all be taken into account when comparing incidence and prevalence rates between countries. Within these constraints, however, the rise in ESRD in Europe has mirrored that in the United States, despite lower absolute rates. Western Europe experienced a linear rise in incidence rates of about 4.8% per year [5]. Similar to what happened in the United States, rates rose more quickly among males than among women and were more pronounced among older age groups [6]. Between 1982 and 2001, the annual incidence rate of ESRD almost tripled in Japan.

Over the past few years, Taiwan's unadjusted rate has increased at a nearly double-the-U.S. rate, similar to that of the United States [7]. In comparison to the aforementioned figures, the unadjusted incidence rate in Australia and New Zealand is significantly lower [8]. Due to the high incidence of ESRD in black Americans, some countries have lower ESRD incidence rates than the United States. Additionally, it is evident that CKD prevalence rates are high in low-income nations like Pakistan, where access to ESRD treatment is either nonexistent or extremely limited [9]. Due to both higher incidence rates and greater survival rates, the prevalence of ESRD in the United States has steadily climbed over the past few decades. The rise in the percentage of patients receiving dialysis on a regular basis can be attributed to better survival rates. The pace of increase has

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stabilised more lately, with recent yearly increases of about 5% per year, as demonstrated in the incidence rate. The prevalence of hemodialysis patients' yearly rate of growth decreased from 8.7 percent in 1997 to 3.7 percent in 2008, whereas the prevalence of peritoneal dialysis patients had their first increase since 2003, rising 1.3 percent in 2008 [2].

In addition, even with the incidence rate stabilising, it is predicted that by 2015, the incidence (95% CI) rate for ESRD will have grown to 136,166 cases per year [10] due to anticipated demographic changes in the general population as well as the ongoing rise in diabetes. The prevalence of CKD in the general population, the rate at which CKD progresses to ESRD, the rate at which patients are accepted into renal replacement programmes, and the effects of competing causes of mortality that cause patients to pass away before beginning dialysis will all affect the incidence of renal replacement therapy. Additionally, the relative impact of these many factors in relation to an increased incidence may vary significantly by race [11].

Different countries have different treatment options for ESRD. For instance, home dialysis is frequently used in the United Kingdom, Australia, and Canada, while it is not widespread in Japan [7]. Furthermore, there are significant regional differences in kidney transplantation. The acceptance of living donation or brain-death criteria in society, as well as legislative restrictions and cultural hurdles, are significant factors of national transplantation rates. Even though it's considered negatively, everyone will eventually pass away. Some people in many religions think that when you die, you enter a new spiritual world. Because of this, certain religious doctrines such as Judeo-Christian, Tibetan Book of the Dead, Buddhist, and Methodist allow patients to reject therapy [12].

Population with ESRD Demographics

Each year, the United States Renal Data System (USRDS) releases updated demographic data regarding the ESRD. The number of patients receiving maintenance dialysis in the United States grew from 275,000 in March 2002 to 520,000 in 2010 [13]. As the average age of dialysis patients rises, around half of them are now above the age of 65. The average age of a patient starting dialysis is also significantly lower in developing countries than it is in developed ones, which is a feature of developing countries in general. Historically, dialysis may not have been offered to or accepted by older individuals, especially those with major comorbidities. Recently, whether as a result of improved management of comorbidities, higher patient expectations, or greater availability of renal replacement therapy, this has substantially changed.

Additionally, men (53% men, 47% women) and people of colour are more likely to have ESRD. Men have a greater age- and race-adjusted incidence of ESRD than women, and this difference has gotten worse with time. Further research is necessary to determine if the lower incidence of ESRD in women relative to males is a true physiologic effect of gender or the result of underdiagnosis or undertreatment of ESRD in women. Additionally, the adjusted ESRD incidence rate varies significantly by race, with African Americans having a 3.5-fold higher incidence rate than do whites after adjusting for age and gender [7].

The incidence rate of ESRD has significant geographic variation as well, with urban areas seeing greater rates than rural ones. The mobility of patients receiving treatment from rural to urban environments or to limited access to care in rural settings, with reduced opportunities for disease recognition and management.

The most frequent causes of ESRD are diabetes mellitus and hypertension (40% and 28%, respectively). The underlying aetiology of chronic kidney disease in the US, Iran, and Saudi Arabia is displayed in Table 1 [14]. Due to late referral of patients and other factors, it appears that CKD of uncertain aetiology is more commonly reported in developing nations restricted infrastructure to timely interventional procedures, including kidney biopsy, for underlying diseases identification. This could explain why some nations, like the Islamic Republic of Iran, have a low prevalence of glomerular disease, which is mostly identified through kidney biopsy. In order to produce statistical data on this issue that are more precise, advanced diagnostic tools and expertise are necessary.

Table 1: Causes that are at the root of chronic kidney disease (CKD)

| Cause | Prevalence (%) | | |
|----------------------------|----------------|------|--------------|
| | United States | Iran | Saudi Arabia |
| Diabetes Mellitus | 40 | 26.8 | 25.2 |
| Hypertension | 28 | 13.5 | 30.4 |
| Glomerular Diseases | 12.2 | 6.5 | 12.5 |
| Cystic Kidney Disease | 3.3 | 10.3 | 4.5 |
| Tubulointerstitial Disease | 3.9 | 1.5 | 1.8 |
| Unknown Etiology | 9 | 29.5 | 19.9 |

While incidence of ESRD caused by glomerulonephritis have decreased among Americans under the age of 40, both whites and African Americans, the same cannot be said for ESRD caused by diabetes and hypertension in people between the ages of 20 and 39. African Americans' linear rate of increase in diabetic ESRD is particularly significant, in part because it contrasts with whites' linear rate of decline, which has decreased to the level reported 15 years ago. Greater levels of obesity in the general population and among minorities are linked to potential variables influencing the increased prevalence in African Americans and other minority communities. Although younger individuals now account for a higher percentage of incidence ESRD owing to diabetes, they have been stable or falling in older populations and whites, showing that a detailed assessment of subpopulations is required to determine whether trends are consistent across all groups defined by age, gender, race and primary cause of ESRD [2].

Getting Ready for and Starting Renal Replacement Treatment

Knowing whether patients need renal replacement treatment is crucial because careful planning can reduce morbidity and death. Early detection enables dialysis to begin at the ideal time and may also enable family members to be evaluated for kidney transplantation before the necessity for dialysis. Additionally, enough time must pass for the ESRD patient to psychologically accept the need for ongoing renal replacement therapy [15].

Advisory about Nephrologists

The field of nephrology includes both primary (medically unrelated to the kidneys) and specialised medical care. There are certain debatable aspects of a nephrologist's primary care, such as [16]:

- The time and expertise necessary for primary care.
- The insufficient payment for non-dialysis-related care.
- The access to nephrologists.
- Upcoming worldwide capitation systems for dialysis care

The impact of nephrologists serving as primary care doctors on the morbidity and mortality of ESRD patients is little understood. The results of patients may be influenced by the doctor's experience in some cases, but not in others, according to some data [17]. Nephrologists do provide primary care for their dialysis patients in clinical practise, however as the number of people with end-stage renal illness rises, this role may be less frequently taken up by nephrologists.

Effectiveness and Cost

There is little data on the effectiveness and financial advantages of nephrologists versus internists in the management of ESRD patients [18]. According to one research of 174 hemodialysis patients, care by a nephrologist was linked to a much shorter hospital stay, cheaper expenditures, and several lines of therapy. Numerous pieces of data back up the assertion that the time of a patient's referral to a nephrologist affects the outcome and cost of dialysis [19]. Thus, patients with chronic kidney disease should be referred to a nephrologist at an early stage of the illness, ideally before the plasma creatinine concentration exceeds 1.2 and 1.5 mg/dL in men and women, respectively, or the eGFR (estimated glomerular filtration rate) is lower than 60 mL/min per 1.73 m² [20].

Conclusion

The epidemiology of chronic kidney disease has progressed to the point that it now acknowledges the significant frequency of the earliest phases of CKD, which are characterised by kidney damage and mild decreases in GFR. The epidemiology of treated renal failure is more developed, and freely accessible statistics internationally demonstrate a gradual rise in all nations, therefore it is anticipated that the overall number of cases requiring dialysis will continue to rise sharply. Patients who begin dialysis sooner rather than later [36] and voluntarily rather than involuntarily experience better outcomes. However, according to other researchers, starting dialysis early did not result in better clinical or survival results for patients with stage 5 chronic renal disease [21]. The backbone of treatment for end-stage renal disease (ESRD) and the rising numbers of ESRD patients worldwide present a challenge to healthcare providers to optimize treatment outcomes in the most cost-effective manner. The results of the HEMO Study, in which increasing the delivered dose of dialysis or using high-flux dialyzer membranes did not improve mortality, suggests that new approaches will be required to improve overall mortality and morbidity rates in this modality [22].

Hemodialysis makes an effort to duplicate glomerular filtration, although it does not take the place of renal tubular function. To reduce uremic toxicity, tubular processing of glomerulofiltrate through selective metabolism and transport may be crucial.

For the treatment of individuals with renal failure, cell-based treatments that provide proximal tubular function are currently being developed. In the end, renal organogenesis, whether partial or total, may result in successful renal replacement therapy without the allogenicity or xenogenicity connected with heterotopic transplantation [23].

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