CURRENT STATUS OF END-STAGE RENAL DISEASE CARE IN SOUTH ASIA

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Of the 1.5 million people of South Asia, a large number live in extreme poverty in rural urban areas and have limited access to health care. End-stage renal disease (ESRD) is a devastating medical, social, and economic problem. Lack of registries prevent an accurate assessment of the incidence or prevalence of ESRD, but a recent population-based study assessed the age-adjusted incidence at 232 cases per million population per year. ESRD treatment facilities are available only in major cities, requiring many patients to travel long distances to seek care. Many patients never come to medical attention.

Until recently, infection-related glomerulonephritides were considered the most common cause of ESRD, but recent years have shown rapid emergence of diabetic nephropathy as the most frequent cause among new ESRD patients who are younger compared to their Western counterparts. A large number presents with a short history of ESRD of undetermined etiology and often require emergency dialysis. Non-availability of health insurance limits the ability of patients to afford costly ESRD care. The quality of chronic dialysis is dictated mostly by non-medical, financial factors. Maintenance hemodialysis (HD) facilities are scarce. Chronic peritoneal dialysis is not cheaper than HD; high cost and nephrologist bias have limited the growth of peritoneal dialysis in South Asia.

Transplants using organs from a related donor is the only viable form of renal replacement therapy for the majority. Cost issues and lack of an effective deceased donor program have limited its availability. Improvement in ESRD care would require strong support from the government, awareness on the part of the medical community of the need of timely referral of these patients to the nephrologist, appropriate pre-dialysis education and development of a network of integrated ESRD treatment facilities for optimal utilization of all forms of renal replacement therapy so that the outcomes of these patients can be improved. (*Ethn Dis*. 2009;19[Suppl 1]:S1-27–S1-32)

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INTRODUCTION

India, Pakistan, and Bangladesh comprise the South Asian region; this region is home to ≈1.45 billion people who share common ethnic origins, cultural heritage, and are approximately at the same stage of economic development. Most of the population in this part of the world lives in rural areas, and the economy is mostly farm-based. Recent years have seen impressive economic growth in some parts of India and to a lesser extent in Pakistan, but great economic disparities continue to be evident within the societies living in these countries. Whereas the number of affluent persons has grown considerably, a large proportion is desperately poor, and most live in rural areas and urban slums. The latter frequently exist in proximity to highly developed localities in the metropolitan cities, and their population is growing rapidly as people come to cities from villages in search of work. The mean per capita gross national product has grown, but still ≈.7 billion people continue to live on <$1/day, and another .5 billion are only slightly better off.[1] Table 1 shows the economic and development indicators of major South Asian nations.

Also common to these countries are the challenges in providing appropriate health care, including to patients with end-stage renal disease (ESRD). ESRD is a devastating medical, social, and economic problem for patients and their families. The initial diagnosis and recognition of the need for continuous and expensive therapy make patients feel vulnerable, dependent, and near death. In contrast to rest of the world, where the stress is on improving quality of life and long-term survival through effective renal replacement therapy (RRT), the enormous costs of therapy limit the continuation of treatment in these countries.[2]

ESRD INCIDENCE AND PREVALENCE

Until recently, a reasonable estimate of the number of persons who need RRT was not possible because of the lack of registries or other data collection facilities in the region. Most of reported data were hospital-based and rough estimates based on individual experience.[2–5]

A recent study[6] has filled this gap. This study was conducted at a hospital in the city of Bhopal in central India in 2000 by the order of the Supreme Court of India to take care of persons potentially exposed to the methyl-isocynate gas that had leaked from the Union Carbide Plant as a result of an industrial accident in 1984. This hospital provides free medical care, including RRT, to ≈570,000 persons, all of whom carry a unique identification card. We determined the annual ESRD incidence rate between 2000 and 2004 in this population. Table 2 shows the summary of findings. The crude and age-adjusted ESRD incidence rates were consistent during this period and were determined at 151 and 232 per million population (pmp), respectively. If these figures are validated in other parts of this region, it would mean that 250,000–300,000 new patients need RRT every year in this part of the world.

The prevalence of ESRD across the nation is much more difficult to estimate. This is because of the disparities in the locations of hospitals equipped to care for ESRD patients.

Table 1. Economic and development indicators of major South Asian nations[1,15]

Indicator	India	Pakistan	Bangladesh	Sri Lanka
Population, in billions	1.13	.16	.15	.021
Percent living in urban area	28.5	34.5	24.7	15.2
Birth rate, per million	22.7	27.5	29.4	17.0
Population growth rate (%)	1.6	1.8	2.1	1.0
Median age (years)	24.8	20.9	22.5	30.0
Infant mortality rate (per 1000 live births)	34.6	68.9	59.0	19.4
Life expectancy at birth (years)	68.6	63.7	62.8	74.8
Literacy rate (%)	61	50	43	91
Per capita GDP ($)	640	632	406	1033
Per capita GDP (PPP) ($)	3139	2225	1870	4390
Percentage living below national poverty line	29	33	50	25
Health expenditure per capita (private and public, PPP $)	82	48	68	121
Health expenditure per capita (public, % of GDP)	1.2	.7	1.1	1.6
Resources consumed by the top 10% of the population (%)	34	28	27	40

GDP = gross domestic product, PPP = purchasing power parity.

Such hospitals are located almost exclusively in major cities. Patients therefore have to travel far from their places of residence to such hospitals, often to different states and even to different countries. Thus, it is impossible to estimate the prevalence of ESRD in the areas where these hospitals are located. Approximately 65%–85% of the population lives in villages, many of which are not easily accessible by rail or road. Indeed, many patients never come to medical attention because local care is not available and the patients lack resources to travel to specialized centers.[5]

A couple of studies have reported on the prevalence of chronic kidney disease in different Indian communities. Mani[7] reported a prevalence of chronic renal failure of .16% and other renal diseases (short of renal failure) in .7% among a rural population of 25,000 near Chennai who are served through a prevention program. Agarwal et al[8] screened >4900 persons in urban communities of Delhi and found a .79% point prevalence of persons with serum creatinine >1.8 mg/dL. These figures are substantially less than those reported from industrialized nations but, because of the sheer size of the population base, represent a substantial burden on the local medical community.

DEMOGRAPHICS OF ESRD

Until ≈10 years ago, glomerulonephritis and interstitial diseases were thought to be the most common causes of ESRD in South Asia.[9] The high prevalence of glomerular diseases was linked to prevalent infections, and interstitial nephritis to environmental toxins. Obstructive nephropathy is common in regions known as "stone belts." Differences in etiologies are also reported according to socioeconomic status, the stage at which the patients present, and the available diagnostic tools. In many instances, renal failure is far advanced at the time of presentation, making the task of guessing the primary disease difficult. These patients typically present with a relatively short history, little or no edema, mild hypertension, and advanced kidney failure with small, smooth kidneys. A similar presentation has been described among South Asians living in the United Kingdom.[10] In recent years, diabetic nephropathy, restricted earlier to high-income groups and older persons, has emerged as the most important cause and accounts for >40% of all new ESRD cases.[6] This has paralleled the rise in the prevalence of type 2 diabetes in the general population, especially in the areas undergoing rapid urbanization.[11] Table 3 lists the cause of ESRD in India and Pakistan.

Compared to the rest of the world, the mean age of patients who require RRT in South Asian countries is much lower.[6,9] This is likely related to the poor availability of health care, which delays diagnosis and leads to loss of opportunities to institute timely preventive measures, such as control of hypertension and dietary modifications, culminating in faster progression to ESRD. The ESRD population in these countries is made up of persons in the most productive years of their lives, often the sole wage earners of families with multiple dependents. These patients often arrive in a morbid condition with advanced uremia, with complications involving multiple organ systems, and in need of immediate dialysis.

Table 2. Incidence of ESRD among 570,000 persons in Bhopal, India, 2002–2005

Factor	2002	2003	2004	2005
New ESRD cases	86	82	85	93
Incidence (pmp)	150	143	149	163
Age-adjusted incidence (pmp)	232	186	317	181
Sex ratio (male/female)	55/45	63/37	65/35	52/48
Mean age (years), ±SD	46±15	50±10	47±13	46±12
Diabetic nephropathy (%)	47	43	40	46

ESRD = end-stage renal disease, pmp = per million population, SD = standard deviation.

DELIVERY OF ESRD CARE

The Indian constitution has provisions that guarantee the right to the highest attainable standard of health

Table 3. Causes of ESRD in India and Pakistan

	India (*N*=1612)*	Pakistan (*N*=4392)#
Chronic glomerulonephritis	27%	14%
Diabetic nephropathy	23%	37%
Chronic interstitial nephritis (including nephrolithiasis)	17%	6%
Autosomal dominant polycystic kidney disease	3%	2%
Hypertension	3%	33%
Unknown and others	17%	7%

Data from *consecutive patients presenting to the Postgraduate Institute of Medical Education and Research, Chandigarh, a public sector hospital in India and #the Dialysis Registry of Pakistan.

care for its citizens. After independence, a commitment to spend 12% of the gross national product on healthcare was made. The government started national programs directed toward controlling infectious illnesses and deficiency disorders. As health was placed under the purview of the state (provincial) governments, substantial differences developed over time in selection of priorities and budgeting, leading to lack of uniformity in the final delivery of care to the people.

The public sector health care is organized in the shape of a pyramid, with primary health centers as the basic units, followed by block- and district-level hospitals and teaching hospitals. The top is formed by tertiary care referral institutions. ESRD care is available only at university or higher-level hospitals. Because of the lack of a formal system of referrals, patients have the freedom to go to any hospital in the country. Hospitals are funded through a fixed annual budget, and it is up to each hospital to divide the funds for different programs. The current annual expenditure on health care by union and state governments totals 1.2% of the total gross national product ($7.6 per capita/year).[1] Most of this amount goes toward meeting the national programs, family planning and nutrition, staff salaries, and maintenance of basic hospital infrastructure. The average primary health center spends ≈$75 every year on medicines and equipment.[12]

The scope of services provided by specialized hospitals is also limited. Patients are not charged for physician advice, hospitalization, investigations, and surgical procedures. The budget, however, is not enough to provide drugs or disposables, and the patients have to pay for these out of their own funds. The insufficient number of major hospitals results in overcrowding and long wait times (often stretching to several months) for specialized procedures like dialysis or kidney transplantation. Patients have to travel long distances, often in excess of 1000 km, to reach government-subsidized hospitals. Families are forced to relocate, leading to loss of livelihood and affecting the education of school children.[3]

The inability of the states to provide adequate health care for the people has led to proliferation of for-profit private hospitals. In general, the larger corporate hospitals provide better care to patients, and many advertise international standards. The available equipment is more modern and better maintained than most government hospitals. Patients, however, pay steep charges that only the rich can afford. A few hospitals are run by charitable organizations, with some assistance from the government. The charges are less than those of private hospitals, and some provide free treatment, including drugs, for a limited period.

Lack of trained manpower hampers delivery of quality health care. The number of nephrology training centers has increased in the last few years, but a substantial proportion of doctors leave to seek work in more affluent Western nations after qualifying. India currently has ≈800 (.7 pmp) nephrologists and adds 20–25 every year. Approximately 750 dialysis units are located in 150 cities (the numbers are constantly increasing) with >3500 dialysis stations and ≈150 transplant centers. Less than 20% of the hospitals are in the public sector, whereas the remaining number are under private management. The more industrialized western and southern states have more RRT centers, whereas the least developed states in the eastern part of India have fewest centers. Pakistan had 140 dialysis centers in 2004, which increased to 195 in 2005. They are spread over 53 cities; ≈30% are government funded, and 45% are under private management. The rest are run by community support or charitable agencies. Approximately 10%–15%, however, are nonfunctional.[13] In both countries, a large number of dialysis units, especially the new ones, are small, minimal-care facilities with fewer than 5 dialysis stations. Many units are looked after by non-nephrologists or even technicians (who also own the unit).

FINANCIAL AND REIMBURSEMENT ISSUES

ESRD treatment presents a study in medical cost-effectiveness. Financing remains the major hurdle for development of RRT facilities in South Asia and is compounded by the lack of a government policy for treating emerging chronic diseases.

The exact cost of RRT in developing countries is hard to estimate and varies with the prescription and the way a unit is set up. The overall treatment cost, though less in dollar terms than that in the developed countries because of lower staff salaries and the low cost of drugs, is still 10–20 times higher than the per capita gross national product and remains out of reach of most of the population. Addition of the cost of drugs like erythropoietin and vitamin D analogs or posttransplant immunosup-

pression raises the RRT costs by >100%. The poor clinical status of the patients necessitates frequent and often long-term hospitalizations. Poor hygiene, a hot and humid climate, and overcrowding predispose these patients to a variety of life-threatening infections. It is estimated that 12%–18% of all dialysis and transplant patients develop tuberculosis.[5] Repeated hospitalizations and prolonged treatment represent an additional financial burden.

Unlike the Western nations, the concept of health insurance (both government funded and private) is in a primitive stage. The costs of RRT, therefore, have to be borne by patients out of their own funds.[4] Some government and private organizations cover the cost of treatment of employees and their dependants as part of employment benefits. Reimbursement policies, however, vary in terms of the amount and duration of coverage. Inpatient treatment is usually paid, but outpatient treatment is not covered uniformly. This effectively eliminates outpatient hemodialysis, chronic peritoneal dialysis, and posttransplant immunosuppressive therapy from the ambit of reimbursement.

The subsidy provided by government hospitals is difficult to calculate.[4] The expenses incurred in setting up and maintaining the units and the staff salaries come out of the global hospital budget. This amount can vary widely depending on the size and location of the hospital, number of dialysis machines in the unit, and university or local affiliation. Furthermore, government hospitals are able to accept only a limited number of patients for RRT. As most large, public hospitals have active transplant programs, patients who are thought suitable for transplant are preferentially accepted. The others are put on a wait list and need to get dialysis in the more expensive private hospitals. The charges in these hospitals vary depending upon the hospital size, type (single or multiple specialty), location, reputation, and additional facilities. Government organizations do not reimburse the higher costs incurred by patients in private hospitals. In recent years, certain organizations have started negotiating reimbursement rates for their employees with private hospitals. Charitable organizations and government administered ''relief funds'' provide limited assistance to poor patients getting treatment in a government hospital. Generally, such assistance will cover 2–3 months of treatment. One study[7] estimated that approximately two-thirds of patients took help from employees or accepted charity, one-third sold property or family valuables such as jewelry, and one-fourth took loans to cover the cost of RRT. Many patients raised funds in more than one way. Only 4% were able to cover the cost with family resources.

HEMODIALYSIS

Mass-based hemodialysis programs are virtually nonexistent in South Asia.[5] Almost all ESRD patients receive hemodialysis for a few weeks after diagnosis, but only the affluent are on hemodialysis for long periods. Units in government hospitals have to cater to a large load of patients with acute renal failure, imposing a limitation on the number of patients who can be provided long-term hemodialysis at subsidized rates. Setting up new units or expansion of existing units is difficult because of high infrastructure cost. The decision on the frequency and duration of dialysis rests on patient symptoms and financial considerations. The prevalent practice is to provide one to two 4-hour sessions every week. Dialyzer reuse is almost universal and often performed manually. It is not uncommon for patients to reduce the dialysis frequency as financial resources dwindle, leading ultimately to discontinuation of dialysis or death.[2] In a cohort of >1200 consecutive ESRD patients referred to my (public sector) hospital, the mean hemodialysis duration was <1 month. Approximately 10% of patients died in hospital and another 60% left the program and were lost to followup. Only 2% were on hemodialysis for more than 6 months. Long-term survivors on hemodialysis are rare, and even they are seldom free from symptoms. Most patients are poorly rehabilitated. The absence of regulations by the government or professional societies has prevented standardization of dialysis treatment, including those for dialysis machines, quality of water used for dialysis, type of dialyzers, and reuse policies.

PERITONEAL DIALYSIS

The limited funding available for setting up HD facilities, coupled with the advantage of being practiced in remote areas, makes chronic peritoneal dialysis the theoretically preferred form of RRT in South Asia. After initial training, the patient is no longer dependent on regular visits to a dialysis center. Despite these obvious advantages, peritoneal dialysis continues to be grossly underutilized. One reason is the continued high cost of peritoneal dialysis systems, almost equivalent to that of hemodialysis. Other issues are delayed presentation to dialysis units, which gives insufficient time for patient education and the preparation required for peritoneal dialysis, and nephrologists' training and bias, especially in the case of those who have their own hemodialysis units. Concerns are often raised about the use of peritoneal dialysis on the grounds that poorly educated patients are likely to be noncompliant and the specter of infection due to the hot, humid climate and poor hygienic conditions. As a result, peritoneal dialysis is seldom offered as a first choice dialysis therapy, and only patients with multiple co-morbidities, not suitable for hemodialysis, are initiated on peritoneal dialysis. This culminates in high initial

dropout rates. More than 4100 patients were initiated on peritoneal dialysis in 2006 in India, but ≈2350 also stopped the therapy during the year. Almost 30% of all dropouts occurred within 6 months of initiation; most of them died due to co-morbidities, indicating that the patient selection might have been suboptimal. As with hemodialysis, the peritoneal dialysis prescription is tailored according to the financial situation. More than 90% patients are on three 2-L daily exchanges. Currently, the number of patients on chronic peritoneal dialysis in India and Pakistan is ≈4500 and 100, respectively.

KIDNEY TRANSPLANTATION

Constraints in running an effective maintenance dialysis program leave renal transplantation as the only viable option for ESRD patients. However transplantation activity falls woefully short of demand; lack of finances, lack of an organized cadaver donor transplant program, and social and religious issues (in some areas) are the major stumbling blocks.

Cadaver donor source is poorly used because of absent or ineffective organ procurement network, lack of facilities for taking care of potential donors, and poor public education. The process depends on the initiative of individual transplanting physicians and cooperating intensive care units. Even though >70,000 road fatalities are recorded annually in India, lack of prompt transport and availability of life-support precludes donation, even in a situation where the families could be approached for consent.[4]

Affordability remains a major barrier for running large transplant programs in developing countries. Even though patients do not have to bear hospitalization costs in state-subsidized hospitals, the cost of immunosuppressive therapy is not reimbursed. Modern drugs like antibody induction or prophylaxis for cytomegalovirus infection are rarely used. Patients are forced to discontinue expensive drugs like calcineurin inhibitors, which leads to high rates of graft loss. Steroid-resistant rejection and viral (cytomegalovirus, BK virus) infections often go untreated.

The worldwide shortage of organs gave rise to the practice of purchase of kidneys from poor persons by affluent persons in India in the 1980s and early 1990s.[14] The buyers came both from within and outside the country, giving rise to the term "transplant tourism." The donor exploitation and substandard medical care provided to recipients was widely condemned and prompted the enactment of an act by the Indian parliament in 1994, officially banning this practice. Since then, it has been practiced only clandestinely in India but is more open in some parts of Pakistan, which does not have such laws. Advertisements can be found on the internet advertising such transplants for $15,000–$20,000.

FUTURE OUTLOOK

Even within the constraints imposed by the economy, a few measures can help expand the scope of dialysis. These include indigenous manufacture of dialysis machines, water treatment system dialyzers, PD fluid bags, and low-cost cyclers and effective reuse of disposables. On the part of physicians and nephrologists, timely preparation of the patient for RRT, including counseling regarding the choice of therapy, management of comorbid conditions, appropriate nutritional intervention, early creation of an atrioventricular fistula or insertion of peritoneal dialysis catheter, and preemptive transplantation where possible, would help in reducing patient morbidity and mortality. In view of the advantages in resource-poor settings, a peritoneal dialysis–first policy, with judicious shift of selected patients to hemodialysis, holds a lot of attraction.

Governments need to realize that ESRD is taking a big toll of its young population and formulate strategies to provide care for chronic kidney disease, including to those with ESRD. Recent years have seen the emergence of the discipline of "preventive nephrology" that emphasizes early detection of kidney disease and institution of measures to slow down its progression. While this very desirable and timely approach would certainly help reduce the burden of disease, it is not going to eliminate ESRD. Without government support, ESRD treatment programs cannot reach the masses, even in affluent nations. Innovative and affordable health insurance schemes that collect small regular contributions (in one instance, 5 or 10 cents per person every month) have been started in parts of India and can bring RRT closer to the common citizen and remove its tag of an "elite therapy."

Development of transplant programs in public-sector hospitals should be encouraged because they are cost-effective and hence accessible to the general population. Cadaver kidney transplants have to be promoted to improve the supply of organs. This would require improvement in hospital infrastructure and educating the public and providers. Predominance of living related transplants in the foreseeable future presents opportunities to find strategies to minimize immunosuppression in well-matched transplants. Another approach is to use drugs that suppress the metabolism of costly immunosuppressive drugs, allowing reduction of drug dose and leading to cost savings.

The quality of health care is inextricably linked to the social and economic development of the societies, and the inequities in access to RRT will persist while the economic disparities remain.

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