

than 10 percent of patients with kidney failure receive any kind of renal-replacement therapy. Although the number of hemodialysis centers is increasing in many regions of Pakistan, most patients who begin to receive dialysis die or stop treatment within the first three months because of cost constraints. Kidney transplantation is the cheaper option, but only about 5 percent of patients with kidney failure receive a transplant. The shortage of donors is a universal problem, and paid organ donation accounts for 70 percent of all transplantations in Pakistan.

Clearly, programs to prevent chronic kidney disease and to treat it in the earliest stages must be designed and integrated into the existing health care infrastructure. The World Health Organization's Innovative Care for Chronic Conditions Framework provides a model for redesigning health care systems in accordance with local resources. The framework emphasizes a well-defined care plan, self-care, scheduled follow-up appointments, monitoring of outcomes, adherence, and step-wise treatment protocols delivered mainly by primary care practitioners. However, increased referrals from such programs, even if limited to patients with advanced disease, may place excessive de-

mands on existing nephrology services. At present, there are only about 80 formally trained nephrologists in Pakistan for a population of about 160 million (the United States has more than 5000 nephrologists for a population of about 300 million). Capacity-building efforts are therefore needed to train physicians in this specialty.

Until the public health services in Pakistan are developed further, private primary care practitioners will continue to be the frontline caregivers in Pakistan. These physicians should be required — perhaps even as a prerequisite for the renewal of licensure — to participate in continuing medical education programs regarding the management of hypertension, diabetes, and chronic kidney disease.

Ideally, developing countries would have access to ample resources to set up large-scale, integrated programs for the prevention and treatment of chronic diseases, as well as dialysis and transplantation units for patients with kidney failure. But in reality, such resources are unlikely to be found. Low-income countries must therefore shift their emphasis from renal-replacement therapy to more cost-effective preventive services, recognizing that questions of social justice and equity will inevitably arise. Since Pakistan's

resources are currently being directed toward the rehabilitation of survivors of October's earthquake, it is unlikely that more resources will be allocated for the treatment or prevention of chronic kidney disease anytime soon. International agencies must therefore recognize that without urgent attention to the problem, the adverse consequences of hypertension, diabetes, and chronic kidney disease will bring untold misery to the next generation of inhabitants of the Indian subcontinent — who represent one sixth of the world's population.

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## Chronic Kidney Disease in the Developing World

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The attention being paid globally to chronic kidney disease is attributable to five factors: the rapid increase in its prevalence, the enormous cost of treatment, recent data indicating that overt disease is the tip of an iceberg of covert disease, an appreciation of its major role in increasing the risk

of cardiovascular disease, and the discovery of effective measures to prevent its progression. These factors render chronic kidney disease an important focus of health care planning even in the developed world, but the problems they delineate in the developing world are far more challenging. Some 85 per-

cent of the world's population live in low-income or middle-income countries, where the clinical, epidemiologic, and socioeconomic effects of the disease are expected to be the greatest.

Data from the United States suggest that for every patient with end-stage renal disease (ESRD),

there are more than 200 with overt chronic kidney disease (stage 3 or 4) and almost 5000 with covert disease (stage 1 or 2). Unfortunately, this type of information is lacking for most other countries, so international comparisons must be based on ESRD, rather than chronic kidney disease.

The prevalence of ESRD is influenced by both the number of new patients requiring renal-replacement therapy (incidence) and the number of deaths. Incidence typically reflects the interaction of genetic and environmental factors, as well as the efficacy of primary health care services. Mortality, for its part, is directly related to the technical and organizational competence of programs offering renal-replacement therapy. With the improvement of such therapy, the known prevalence of ESRD continues to increase in most countries: it is currently higher than 2000 per million population in Japan, about 1500 per million population in the United States, and about 800 per million population in the European Union. In developing countries the figures vary, from less

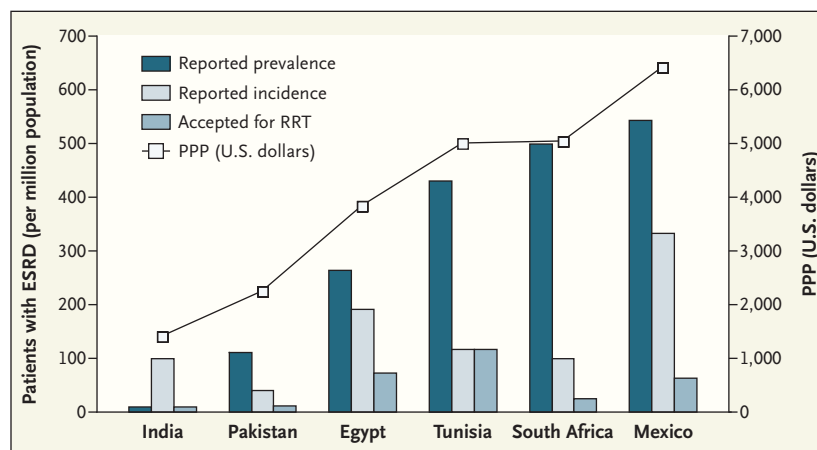
than 100 per million population in sub-Saharan Africa and India to about 400 per million population in Latin America and more than 600 per million population in Saudi Arabia, despite similar rates of incidence in these countries and regions. Thus, prevalence is largely a matter of survival made possible by renal-replacement therapy, which, in turn, is dependent on health care expenditures and economic strength (see graph).<sup>1</sup>

Although the credibility of statistics from many developing countries may be questionable, the majority of experts agree that 150 per million population is the average incidence of ESRD.<sup>1</sup> Surprisingly, this figure is lower than those reported in the developed world: in the United States, for example, the incidence is about 330 per million population. The difference reflects genetic and environmental factors: the role of ethnic origin is evident in the fact that the incidence is much higher among blacks and Hispanics in the United States than among their white counterparts, and the effect of environment is reflected by an incidence in these subpopu-

lations that is vastly higher than the incidences among the same racial and ethnic groups in Africa and Europe.

The variation among communities in the incidence of ESRD mirrors that in the prevalence of diabetes, obesity, and hypertension.<sup>2</sup> This observation has worrisome implications for the future incidence of ESRD in the developing world, where the prevalence of diabetes is expected to double by 2030.<sup>3</sup> It is estimated that by that year, more than 70 percent of patients with ESRD will be residents of developing countries, whose collective economies will account for less than 15 percent of the total world economy. Even more disturbing is the thought of the organizational and financial resources needed for the prevention and early detection of chronic kidney disease — requirements that are far greater than those for ESRD, if the proportions of patients in the United States may be extrapolated to the developing world.

Chronic glomerulonephritis and interstitial nephritis are currently the principal causes of chronic kidney disease in developing countries, reflecting the high prevalence of bacterial, viral, and parasitic infections that affect the kidneys. Of the implicated bacterial infections, tuberculosis ranks high in India and the Arabian Gulf, whereas streptococcal infections of the throat and skin remain major causes of glomerulonephritis in Africa. Viral infections are responsible for the high incidence of glomerulonephritis in some regions — for example, hepatitis B virus in South Africa, hepatitis C virus in Egypt, and the human immunode-



**Reported Prevalence and Incidence of ESRD and Rates of Acceptance for Renal-Replacement Therapy (RRT), in Relation to Wealth.**

ESRD denotes end-stage renal disease. Purchasing power parity (PPP) is an economic measure that compares annual incomes per capita on the basis of purchasing power for goods and services. Data are from the World Bank, 2001.

iciency virus in sub-Saharan Africa. Several parasitic infections cause ESRD through ureteric obstruction (e.g., schistosomiasis, in most of Africa), interstitial nephritis (e.g., kala-azar [visceral leishmaniasis], in many African and Asian countries), and glomerulonephritis (e.g., malaria and filariasis, in West Africa; and schistosomiasis, in Africa and Latin America).

The histologic types of glomerulonephritis in the developing world vary considerably. IgA nephropathy predominates in Southeast Asia and the Pacific region (accounting for 35 to 45 percent of cases) but is rare in Africa (accounting for only 3 to 4 percent of cases). Focal segmental glomerulosclerosis is the most common type among the black populations of Africa (15 to 25 percent), Saudi Arabia (40 percent), India (up to 46 percent), and South America (up to 43 percent), probably as a consequence of the low nephron mass associated with low birth weight. Proliferative forms of glomerulonephritis are more homogeneously spread throughout the developing world, accounting for 25 to 35 percent of reported cases.

Diabetes causes 9.1 to 29.9 percent of the cases of ESRD in various developing countries, and hypertension leads to 13 to 21 percent of the cases. Other important causes include urolithiasis with subsequent obstruction and infection, long-term drug abuse, and possibly environmental pollution. The magnitude of pollution's contribution remains questionable: an association has been documented only for occupational exposure to lead, cadmium, and mercury.

The ultimate outcome of chronic kidney disease in many patients

is ESRD, which necessitates ever-growing dialysis and transplantation programs. In addition to placing an unaffordable financial burden on poor countries, renal-replacement therapy has negative sociopsychological effects on communities. In most developing countries, the typical patient undergoing regular dialysis is only partially rehabilitated, since dialysis is often inefficient (due to limitations of technical and human resources); essential treatments such as erythropoietin, active vitamin D, and statins may be in short supply; coexisting conditions such as hepatitis infection, parasitic infestations, and malnutrition are common; and transportation difficulties often result in noncompliance. Families must often cope with a chronically depressed, sometimes aggressive, unemployed relative who must be escorted regularly to a possibly distant dialysis center to receive treatment.

Although many countries with medium-sized economies offer transplantation services, these are unaffordable for most patients. In theory, it should be relatively easy to obtain kidneys from living, related donors in countries known for large, tight-knit families, but calls for donation often meet with a disappointing response, owing to fear, skepticism, or illiteracy. Efforts to increase the donation of cadaveric kidneys are hampered in many developing countries by religious, legal, and social constraints. Such prohibitions have opened the door to the selling of organs from living donors — raising moral and legal issues.

In addition, chronic kidney disease increases the relative risk of cardiovascular disease, which leaps from about 1.5 among pa-

tients with isolated proteinuria to almost 500 among young patients who are dependent on regular dialysis. This enormous risk is attributed to a number of “traditional” factors, such as hypertension and dyslipidemia, as well as to “nontraditional” factors such as hyperphosphatemia, hyperhomocystinemia, and other conditions.

The obvious task ahead for health authorities in the developing world is to detect and treat kidney disease at the earliest possible stage. For this purpose, the International Society of Nephrology has designed guidelines adapted to the developing world.<sup>4</sup> Screening only persons deemed to be at high risk may be a viable option when mass campaigns are impossible. Control of diabetes, hypertension, smoking, overweight, infection, and pollution — and possibly the use of a single daily pill (“polypill”) containing generic angiotensin-converting-enzyme inhibitors, statins, aspirin, and folic acid in order to simultaneously control blood pressure, dyslipidemia, and thrombogenic tendency — should be on the agenda of many developing countries.

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