

The state of nephrology in South Asia

Vivekanand Jha^{1,2}, Harun Ur-Rashid³, Sanjay Kumar Agarwal⁴, Syed Fazal Akhtar⁵, Rishi Kumar Kafle⁶, Rezvi Sheriff⁷, *on behalf of the ISN South Asia Regional Board*

¹George Institute for Global Health India, New Delhi;

²University of Oxford, Oxford, UK.

³ Kidney Foundation Hospital and Research Institute, Dhaka, Bangladesh

⁴ All India Institute of Medical Sciences, New Delhi, India

⁵ Sindh Institute of Urology and Transplantation, Karachi, Pakistan

⁶ Medicare National Hospital & Research Center, Kathmandu, Nepal

⁷ National Hospital, Colombo, Sri Lanka

Corresponding author: Professor Vivekanand Jha, The George Institute for Global Health; 310-11 Elegance Tower, Jasola District Centre, New Delhi 110025 India. Tel: (+91)-11-415-880-91 | Fax: (+91)-11-415-880-90. Email: vjha@georgeinstitute.org.in

Abstract

Kidney disease attributable deaths and disability-adjusted life years have risen rapidly in South Asia. Diabetes is the commonest cause of kidney disease, but a substantial burden of disease is due to unmeasured risk-factors. Supported by governments, dialysis is growing but needs better oversight. The paper describes current service, training and research needs in the region.

Keywords: South Asia, Chronic kidney disease, Dialysis, Registry

The South Asia region of the International Society of Nephrology comprises 8 countries (Table 1) with a combined population of 1.77 billion, about 29% of world population in 2016. The World Bank classifies Afghanistan and Nepal as low-income and Bangladesh, Bhutan, India, Pakistan and Sri Lanka as low-middle income economies while Maldives is an upper middle-income country. Over 65% of the population in the region lives in rural areas.

Table 1 shows the development and health indicators of the South Asian countries. Notable are the relatively low health spending by the governments of three largest countries, the high out-of-pocket expenditure, low physician-to-population ratio (WHO recommended ratio: 1:1000); and high maternal, infant and under-5 mortality rates.

All the countries are characterised by large socio-economic inequities and regularly experience disasters - both natural (earthquakes, floods, droughts) and man-made (wars, conflicts) - which affects healthcare delivery, including that for kidney diseases. All countries in the region are in the bottom half of the list of 191 countries in terms of their Socio-demographic Index, developed by the Global Burden of Disease Study (Table 1).

Although non-communicable diseases (NCD) have taken primacy as the major causes of death and disability throughout the region, with the exception of Afghanistan, national policies for NCD control are in early stages of development and implementation. These policies are targeted to hypertension, diabetes, cardiovascular disease and common cancers. There is no stated policy for kidney disease screening and/or management in any South Asian country.

Kidney disease burden in South Asia

The Global Burden of Disease Study performs regular evaluation of disease burden in all regions of the world and provides modelled estimates for countries that do not have good quality primary data. Table 2 shows the estimated burden of kidney disease in South Asia in 2016 expressed as the numbers of deaths and disability adjusted life years (DALY), the age-adjusted death rate and the change compared to 1990¹. The number of deaths and DALY has increased throughout the region, and more than doubled between 1990 and 2016 in India, Nepal, Pakistan and Afghanistan. The Million Death Study that established cause of death in a million households across India using a verbal autopsy tool, documented a rise of >50% in

the proportion of renal failure deaths to all deaths over a 10-year period (2001-03 and 2010-13)². The rise was particularly notable in the Southern and Western states. Sub-national data are not available for other countries in the region.

Table 3 documents the rise in the incidence and prevalence numbers and rates of individuals with chronic kidney disease (CKD) in South Asia. The rise in the age-adjusted incidence and prevalence rates contrasts with a global trend, which has shown a decline. Deconvolution analysis has shown that most of the increase in the region is driven by population growth.¹ In terms of cause; hypertension, diabetes and glomerulonephritis explain 60-75% rise in the CKD burden, the cause in the rest remains unascertained¹. There is a significant departure from this trend in several parts of South Asia. Pockets have been described in Sri Lanka and India where CKD of uncertain etiology seems to be endemic. Accurate estimation of disease burden, epidemiology and identifying possible causes is a topic of research³. This condition largely affects farm workers who toil in hot and humid conditions and is akin in clinical presentation and course to Mesoamerican nephropathy. This observation suggests the need to develop kidney disease screening policies independent of those for hypertension and diabetes in the region.

The high burden of CKD-attributable deaths in the age range of 40-60 years in South Asia has particular bearing on the economic status of families and societies to which the affected individuals belong, especially when the affected individual is the family bread-winner. According to a study amongst patients with end-stage kidney disease (ESKD) in India, even a short period at dialysis prior to getting a kidney transplantation resulted in catastrophic healthcare expenditure (>40% of non-food expense) in over 80% of patients, with the proportion exceeding 100% in about half, leading to distress financing – such as taking loans, selling of assets, etc ⁴.

The burden of acute kidney injury (AKI) in the region has not been accurately estimated, but published literature indicates it to be high. Most AKI seen in public hospitals is acquired in the community, related to suboptimal sanitation and water quality, tropical infections and poor obstetric care. Delayed recognition and inappropriate treatment in the remote rural areas results in missed opportunities to prevent development of AKI. Delayed presentation to

hospitals that can provide renal support results in high mortality and rates of residual renal dysfunction, as shown in the ISN Oby25 pilot project⁵. An implementation phase of a package of interventions developed in the project is currently underway in Dharan, Nepal.

The landscape of nephrology service policy and manpower in South Asia.

Table 4 shows the current service provisions for patients with kidney disease in the region. These data were collected from published and grey literature, reports in lay press, by surveying nephrology leaders in India Bangladesh, Nepal, Pakistan and Sri Lanka, and through personal contact with people knowledgeable about renal services in Afghanistan, Bhutan and Maldives. This high-level information does not include all metrics, and is unable adequately capture within-country variation.

The shortage of nephrologists throughout the region is evident. Dialysis is growing, with an estimate suggesting growth in excess of 30% per year in India. Sri Lanka, Maldives and Bhutan already have universal dialysis. The proportion of patients for AKI and ESKD who are able to get dialysis ranges from <5% in Afghanistan and parts of other countries to 100 percent in Bhutan and some states in India. The Government of India announced a National Dialysis Service in 2016 to provide free dialysis to citizens below an income threshold, and according to the ability to pay for others, to be provided dialysis through district level dialysis units under public-private partnerships. Analysis of data from one such program that was instituted in 2008 showed that while such state-funded dialysis uncovered unmet need by showing progressive increase in uptake, the outcome was marred by high dropout rates, with about 60% of all subjects stopping dialysis within 6 months⁶. This suggests existence of residual barriers to continued treatment - potential factors being lost wages, transport costs, cost of ancillary medications and management of medical complication and vascular access related issues. Anecdotal reports have also raised concerns regarding the quality of dialysis.

There is no stated policy for determining eligibility to RRT, or choice dialysis modality. Over 95% of dialysis patients are receiving hemodialysis (HD). Recent years have seen setting up of standalone HD units in small towns in India. These units are managed by independent organizations under public-private-partnership that offer economies of scale and

opportunities for standardization of services, quality control and accountability. On the other hand, wars and conflict have prevented expansion of service in parts of South Asia.

There is a widespread perception that HD is cheaper than PD, but a recent health-economic analysis⁷ from India showed the cost of HD to be several-fold greater than what was reported before, emphasizing the need for a proper health technology assessment of both dialysis modalities using the Thai model.

The availability of kidney transplantation is even more limited. Despite being the most cost-effective renal replacement therapy, the number of transplants remains woefully low with respect to those who need it and is dependent on living donors, because of a combination of economic issues and shortage of effective large-scale deceased donation programs. In recent years, some Indian states have experienced an increase in organ retrieval rates from deceased donors. Increasing use of ABO-incompatible transplants, paired donation and swaps have also improved access.

Service provision in the region has been supported by not-for-profit organizations and charitable hospitals. A notable example is the Sind Institute of Urology and Transplant at Karachi, Pakistan (<http://www.siut.org>), that provides free lifelong care to a large number of patients with kidney disease using a model of partnership between government and philanthropy.

Insufficient number and uneven distribution of trained medical and paramedical professionals, properly equipped facilities and lack of guideline-driven treatment impacts all aspects of kidney care in the region. High quality but expensive care is provided in private hospitals to those who can afford it either through personal means or by employment-based insurance. Those without such cover (unorganised workers or self-employed) have to depend upon the limited number of oversubscribed public-sector facilities. Many private hospitals also provide care, especially kidney transplantation, to wealthy foreigners - especially those from Sub-Saharan Africa, middle east and central Asia. From time to time, various centers in India, Pakistan and Sri Lanka have indulged in large-scale commercial transplantation, both for domestic and foreign recipients. These were widely criticized and led to enactment of laws

banning sale and purchase of organs. Clandestine cases of kidney sale continue to be reported, however. Worth pointing out is the intra-regional trafficking, with poor people being brought from Bangladesh and Nepal to India, Pakistan and Sri Lanka for sale of kidneys and rich people from India going to Pakistan and Sri Lanka to be transplanted⁸.

Basic laboratory services (qualitative urinalysis and serum creatinine) are available in most urban areas and are relatively cheap, but assay methodologies (e.g. serum creatinine) are not uniformly standardised. Proteinuria quantitation is available in fewer facilities. Specialized services like renal pathology and transplant immunology are also limited. Non-availability of immunofluorescence and electron microscopy constrains the ability to accurately diagnose and classify kidney disease. Facilities that collect blood and biopsy samples from small towns and have them analysed in central laboratories are improving service availability.

Widespread availability of generic medicines and biosimilars in the region has the potential to bring down the cost of treatment. By way of example, a vial of 4000 units of erythropoietin costs as little as US\$4 in India. On the other hand, some drugs like eculizumab are not available even to those who can afford it, forcing them to buy using clandestine routes.

Nephrology Training and research in South Asia

Active nephrology training programs are present in five countries but the number of nephrologists being produced remains low compared to the need. This is compounded by 'brain-drain' of trained nephrologists to industrialised countries. Training programs for paramedical staff (nurses, technicians) are also inadequate, given the rapidly growing demand. Capacity building in the region has been supported through ISN programs. In partnership with The American Nephrologists of Indian Origin (ANIO), the ISN runs a few special programs in the region (<https://www.theisn.org/programs/isn-anio-partnership>). They are Clinical Nephropathology Certificate Program, initially intended for the region but later opened to wider ISN membership in view of the high demand; the Scientific Writing Academy Course in which aspiring candidates are taught skills in designing, implementing and publishing clinical research in nephrology; and the The Indukaka Ipcowala Advanced Apprenticeship Program, which enables physicians or allied healthcare personnel from India to gain specific skills through practical experience.

National nephrology societies are present in Bangladesh, India, Nepal, Pakistan and Sri Lanka and all are affiliated with the ISN. The Indian Society of Nephrology also has four zonal chapters.

Research in nephrology has been dominated by epidemiological studies describing the pattern of different diseases. In recent years, randomised controlled trials have been conducted for several conditions. Basic laboratory research is limited to a handful of institutions in India, with few PhDs focussing on kidney diseases. Other notable studies have examined the performance of the existing creatinine-based GFR estimating equations in South Asian populations and found them to be inaccurate. In the largely vegetarian Indian population, they overestimate the actual GFR, perhaps related to lower muscle mass. The Indian Chronic Kidney Disease Cohort study⁹, funded by the Department of Biotechnology, Government of India is following and collecting biosamples from about 5000 subjects with early stage CKD, and is a member of the ISN iNET-CKD program.

Funding for research in nephrology is available through government funding schemes in India and to some extent in Nepal and Pakistan. Government of Sri Lanka is supporting research in CKD of undetermined etiology. The Indian Society of Nephrology supports capacity building and research programs in South Asia directly and through partnership with ISN.

There are no active renal disease registries in the region. The Indian Society of Nephrology had initiated a hospital-based cross-sectional CKD Registry which is currently dormant. Efforts to establish national ESKD registries are underway in Bangladesh, India and Sri Lanka.

A recent online survey, sent to over 2400 nephrologists in the region and completed by 334, identified top priorities for the ISN in the region (Fig 1).

To conclude, renal services in South Asia are characterized by increasing disease burden, and a rapidly growing demand for service and research in the face of inadequate financial and manpower capacity. Increasing number of training programs, growing government support

to RRT, availability of cheap generic medicines and development of locally appropriate models of service delivery offer hope for the future of nephrology in the region.

Conflict of interest

VJ serves on Steering Committee for a trial funded by GlaxoSmithKline and serves on an advisory board and/or has spoken at scientific meetings for Biocon, Baxter, Janssen, Medtronic, and NephroPlus. He has a policy of all honoraria being paid to his employer. The other authors declared no competing interests.

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Figure 1:

Survey results for ISN priorities in the South Asia region. Length of bars indicates percent of responders

Table 1: General demographic, economic and health indicators of countries in South Asia

Indicator	Afghanistan	Bangladesh	Bhutan	India	Maldives	Nepal	Pakistan	Sri Lanka
Population (millions)	34.7	162.5	0.8	1324.2	0.4	29	193.2	21.2
Percentage of rural population	73	65	61	67	53	81	61	82
Life expectancy at birth, total (years)	63.7	72.5	70.2	68.6	77.3	70.3	66.5	75.3
Population growth (annual %)	2.7	1.1	1.3	1.1	2.2	1.1	2	1.1
Mortality rate, infant (per 1,000 live births)	53.2	28.2	26.8	34.6	7.3	28.4	64.2	8
Birth rate, crude (per 1,000 people)	48.9	18.9	18.2	19	18.3	19.7	28.2	15.3
Cause of death, by non-communicable diseases (% of total)	33.2	66.9	67.8	60.8	78.4	64.5	56.4	79.7
GDP per capita, PPP (current international \$)	1944.1	3579.8	8245.6	6127.3	14595	2464.4	5235.5	12313
Current health expenditure (% of GDP)	10.3	2.6	3.5	3.9	11.5	6.1	2.7	3
Domestic general government health expenditure per capita (current international \$)	9.5	12.9	207	61	1235	26	37	190
Out-of-pocket expenditure (% of current health expenditure)	78.4	71.8	19.8	65.1	16.4	60.4	34.9	66
Number of physicians (per 1,000 people)	0.3	0.5	0.4	0.8	3.6	0.6	1	0.9
Maternal mortality ratio (modeled estimate, per 100,000 live births)	396	176	148	174	68	258	178	30
Mortality rate, under-5 (per 1,000 live births)	70.4	34.2	32.4	45.2	8.5	34.5	78.8	9.4
Health access quality ¹	26	47.6	47.3	41.2	70.4	40	37.6	70.6
Social development index ²	0.28	0.51	0.59	0.58	0.69	0.45	0.52	0.70

¹Health access quality (0-100): measures personal access to healthcare and its quality, derived from outcomes of 32 diseases that can be avoided or effectively treated with proper medical care

²Social development index (0-1): measures development status of countries based on average income per person, educational attainment and total fertility rate.

Data from The World Development Report 2016 (<https://data.worldbank.org/products/wdi>), the Global Burden of Disease Study 2016 (<http://www.healthdata.org/gbd>), the World Health Organization Global Health Observatory (<http://www.who.int/gho/countries/en/>) and CIA World Factbook (<https://www.cia.gov/library/publications/resources/the-world-factbook/>).

Table 2: Deaths and DALYs attributable to chronic kidney disease in South Asia

Country	Death				DALY			
	Death number (95%CI)	Percentage Change from 1990	Death rate* (95%CI)	Percentage Change from 1990	DALY number (95%CI)	Percentage Change from 1990	DALY rate* (95%CI)	Percentage Change from 1990
Afghanistan	8,047.65 (6,107.86 - 10,520.70)	197.14%	24.09 (18.29 - 31.50)	6.08%	303,585.14 (240,986.39 - 385,770.84)	170.34%	908.89 (721.48 - 1,154.94)	-3.49%
Bangladesh	19,309.40 (17,172.69 - 22,100.74)	34.80%	11.93 (10.61 - 13.65)	-13.25%	597,889.43 - 761,354.99)	3.36%	418.20 (369.31 - 470.29)	-37.81%
Bhutan	116.40 (88.70 - 147.89)	55.45%	14.59 (11.12 - 18.53)	3.51%	958.62 (3,123.42 - 4,885.80)	19.10%	496.11 (391.44 - 612.31)	-20.70%
India	234,345.34 (218,550.67 - 263,799.70)	102.20%	17.81 (16.61 - 20.05)	32.72%	7,672,012.62 (7,093,872.92 - 8,511,010.07)	70.79%	582.96 (539.03 - 646.72)	12.10%
Maldives	70.75 (57.78 - 86.32)	25.48%	19.48 (15.91 - 23.76)	-30.82%	1,748.43 (1,463.97 - 2,116.26) -	19.92%	481.30 (402.99 - 582.55)	-55.85%
Nepal	4,442.31 (3,603.75 - 5,516.60)	103.44%	14.77 (11.98 - 18.34)	26.81%	52,320.59 (126,621.17 - 183,707.93)	60.11%	506.44 (420.99 - 610.80)	-0.20%
Pakistan	29,578.94 (22,568.25 - 41,217.38)	125.28%	15.49 (11.82 - 21.58)	27.75%	1,059,187.18 (839,066.31 - 1,393,716.39)	100.55%	554.67 (439.39 - 729.85)	13.73%
Sri Lanka	4,476.42	84.63%	21.60	54.47%	114,768.35	49.29%	553.91	24.91%

(3,611.48 - 5,477.27)	(17.43 - 26.43)	(95,056.68 - 137,260.96)	(458.77 - 662.46)
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* per 100,000 persons

Source: Xie et al, Kidney Int 2018¹; (data from Global Burden of Disease Study 2016)

Table 3: The incidence and prevalence of chronic kidney disease in 2016 and change from 1990 in South Asian countries

Country	Incidence				Prevalence			
	CKD incidence number (95%CI)	Percentage Change from 1990	CKD Incidence rate* (95%CI)	Percentage Change from 1990	Prevalence number (95%CI)	Percentage Change from 1990	CKD Prevalence rate* (95%CI)	Percentage Change from 1990
Afghanistan	95,665.06 (85,430.26 - 107,258.13)	204.68%	286.41 (255.77 - 321.12)	8.77%	1,191,489.08 (1,076,151.49 - 1,322,367.96)	201.68%	3,567.14 (3,221.84 - 3,958.98)	7.70%
Bangladesh	418,831.07 (374,705.87 - 464,290.14)	108.64%	258.71 (231.45 - 286.79)	34.27%	5,842,741.81 (5,324,591.42 - 6,378,595.38)	118.54%	3,609.03 (3,288.97 - 3,940.03)	40.63%
Bhutan	1,987.09 (1,774.91 - 2,226.54)	79.36%	249.03 (222.44 - 279.04)	19.43%	27,752.18 (25,209.21 - 30,592.90)	90.73%	3,478.01 (3,159.31 - 3,834.02)	27.00%
India	3,349,963.43 (2,956,051.78 - 3,749,342.24)	98.30%	254.55 (224.62 - 284.90)	30.15%	44,099,793.56 (39,990,066.03 - 48,562,284.69)	92.19%	3,350.96 (3,038.67 - 3,690.04)	26.15%
Maldives	493.07 (444.33 - 544.54)	54.78%	135.73 (122.31 - 149.90)	-14.66%	6,946.18 (6,323.53 - 7,558.77)	67.68%	1,912.10 (1,740.70 - 2,080.73)	-7.55%
Nepal	106,355.62 (93,652.50 - 119,600.80)	124.22%	353.61 (311.38 - 397.65)	39.77%	1,456,668.36 (1,314,791.14 - 1,603,419.54)	130.28%	4,843.16 (4,371.44 - 5,331.08)	43.54%
Pakistan	331,921.24	121.36%	173.82	25.53%	4,599,729.69	124.88%	2,408.75	27.53%

	(299,429.68 - 364,867.42)		(156.80 - 191.07)		(4,199,317.26 - 5,059,163.48)		(2,199.06 - 2,649.34)	
Sri Lanka	40,996.72 (36,496.12 - 45,756.88)	99.07%	197.86 (176.14 - 220.84)	66.55%	584,511.75 (529,368.16 - 646,473.78)	94.04%	2,821.03 (2,554.89 - 3,120.08)	62.35%

***Per 100,000 persons**

Source: Xie et al, Kidney Int 2018¹; (data from Global Burden of Disease Study 2016)

Table 4: The current landscape of nephrology service, policy, manpower and training in South Asia

Indicator	Afghanistan	Bangladesh	Bhutan	India	Maldives	Nepal	Pakistan	Sri Lanka
Number of nephrologists	<10	123	1	1,639	<5	50	151	30
Is PD available?								
Acute	Yes, in some cities	Yes, all administrative divisions	No	Yes, all states and union territories	Not known	1/7 provinces	6/8 units	Yes, all provinces
Chronic	No	1/8 administrative divisions	No	21/29 states & 4/7 union territories	No	1/7 provinces	2/8 units	3/9 provinces
Is HD available?	Yes, in some cities	Yes, all administrative divisions	Yes	Yes, all states and union territories	Yes	Yes, all provinces	6/8 units	Yes, all provinces
What proportion of patients who need are able to get dialysis for ESKD	<5%	25%	100%	5-100%	Not known	20%	5-15%	2-12%
Number of patients on chronic dialysis	5000	18,000	140	174,478	Not known	2,877	8,381 (data NA from 2 units)	5,482
Proportion of dialysis patients on PD (%)	0	3	<1	<5	<1	7	<1	
Is Transplantation available?	Sporadic. Patients travel overseas	1/8 administrative divisions. Patients travel overseas	No. Patients travel overseas	In 16 states & 4 union territories	No. Patients travel overseas	1/7 provinces. Patients also travel overseas	5/8 units	4/9 provinces
Is there an active deceased donor program?	No	No	No	13/29 states & 3/7 union territories	No	1/7 provinces	3/8 units	3/9 provinces
Number of kidney transplants in one year	Not known	130	0	6,857	0	312	476	267

Do nephrologists make AV fistulas?	No	Yes, in 1 center	No	Yes, about 40%	Not known	1/7 provinces	Occasionally, 1/8 units	No
Do nephrologists put in PD catheters?	No	Yes, in 1 center	No	Yes, about 20%	Not known	1/7 provinces	6/8 units, mostly acute	Yes, all provinces
Number of dialysis units	<10	101	3	1,584	<5	53	121	29
Number of dialysis machines	200	1179	8	12,881	<40	410	481	274
Number of transplant centers	1	6	0	233	0	4 – all in 1 province	16	7
Funding for dialysis	Private	Mixed	State-funded	Mixed*	Private	State-funded	Mixed	State-funded
Funding for transplant	Private	Mixed	State	Mixed†	Private	State	Mixed	State
What is the OOPE¹ on dialysis/transplant (scale of 0-10)	9**	8		0-10	8	-	3-8	3
Kidney disease treatment guidelines	No	No	No	Yes	No	No	No	No
Number of nephrology training centers	0	6	0	72	0	4	34	9
Number of trainees enrolled in nephrology training programs every year	0	35	0	136	0	5	56	19
National/regional dialysis or kidney disease registries	No	No	No	No	No	No	No	No

*Mixed: various combinations of state funded, employment-based insurance, private insurance, charity (to the patient or dialysis facility), and out of pocket payment.

** state funding started recently.

†Free in public hospitals for the poor; the insured can get in empanelled private hospitals.

¹ ESKD: End-stage kidney disease; OOP: Out-of-pocket expenditure on 0-10 scale, where 0 indicates no OOPE, whereas 10 indicates catastrophic OOPE (>40% of non-food expenditure) and distress financing (loss or sale of assets, borrowing)

Data from survey of academic nephrology centers and leaders using ISN Global Kidney Health Atlas methodology.

