Chapter 130

Chronic Kidney Disease: Current Status, Challenges and Management in India

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INTRODUCTION

Chronic diseases have become a major public health problem. Chronic diseases are a leading cause of morbidity and mortality in India and other low- and middle-income countries. The chronic diseases account for 60% of all deaths worldwide. Eighty percentage of chronic disease deaths worldwide occur in low- and middle-income countries.[1] In India, the projected number of deaths due to chronic disease was around 5.21 million in 2008 and is expected to rise to 7.63 million in 2020 (66.7% of all deaths).[2]

CHRONIC KIDNEY DISEASE: A PUBLIC HEALTH PROBLEM

Chronic kidney disease (CKD) is a worldwide public health problem, both for the number of patients and cost of treatment involved. Globally, CKD is the 12th cause of death and the 17th cause of disability, respectively. This is an underestimate as patients with CKD are more likely to die of cardiovascular disease (CVD) than to reach end-stage renal disease (ESRD). Approximately 30% of patients with diabetes mellitus (DM) have diabetic nephropathy and with the growing number of DM patients and aging population there is likely a parallel increase in CKD incidence. As per the Diabetes Atlas 2006, the number of patients with DM in India (currently around 40.9 million) is expected to rise to 69.9 million by 2025 unless urgent preventive measures are taken.[3] With increasing prevalence of CKD, CKD related excess CVD, ESRD and the consequent financial burden of renal replacement therapy (RRT), the importance of CKD and its risk factors has to be realized. The prevalence of ESRD and patients on RRT has increased over last two decades.[4]

In community-based studies, the CKD prevalence has been reported between 0.16% and 0.79%. The studies were designed to detect stage 3 CKD or worse and the real prevalence of CKD is higher than the reported number.[5-7] The ESRD incidences has been reported to be 160–232 per million population (pmp)[8,9] and the projected ESRD prevalence was 785–870 pmp.[9,10] "Screening and Early Evaluation of Kidney Disease" (SEEK), a community-based voluntary health screening program was started in India in 2006 and tests serum creatinine and urine analysis. SEEK reported a very high prevalence of 17.4% of CKD (unpublished and presented in the Annual Conference of the Indian Society of Nephrology) using an abbreviated modified diet in renal disease (MDRD) formula, a glomerular filtration (GFR) estimation formula.

The Indian CKD Registry, a voluntary reporting body of CKD patients data, initiated in June 2005, has 199 contributing centers. The database has 63,538 patients enrolled, 70% of them males and 73.6% of them have CKD stage 4 and 5. Diabetes is the cause of kidney disease in 30% of these patients. Only 20% of the ESRD registry patients are on some form of RRT. The existing registry has the limitation of being hospital-based and not accurate estimate of population data. The data is available at www.ckdri.org.[11] In summary, the yearly incidence of ESRD in India is approximately 150–200 pmp and DM is an important cause of CKD in approximately 30–40% of the patients. Patients with CKD are likely to die of CVD than to reach ESRD.

PREVENTING CHRONIC KIDNEY DISEASE, END-STAGE RENAL DISEASE, PREMATURE DEATH

Targeted screening identifies the individuals at risk early enough in the course of their disease to allow for effective intervention.[12] Screening for CKD should not be universal but should be performed in individuals at increased risk of developing CKD—DM, hypertension, age more than 60 years, CVD, families' history CKD, hyperlipidemia, obesity, metabolic syndrome, smokers and patients treated with potentially nephrotoxic drugs. The screening tests should include a urine test for proteinuria or albuminuria and a blood test for serum creatinine to estimate glomerular filtration rate (GFR). Initially testing with urine tests for proteinuria or albuminuria is more cost-effective. Initial screening test should be followed by serum creatinine estimation in patients with positive urine albumin.[13] The symptom of CKD develops slow and remains largely asymptomatic. Urine microalbuminuria, especially in patients with DM, detects patients at risk of kidney disease years before they manifest with gross proteinuria or elevated serum creatinine. Estimating GFR from serum creatinine is likely to avoid missing kidney disease at an early stage.[14]

Classical description of diabetic nephropathy has been with initial onset of kidney disease with microalbuminuria, followed by macroproteinuria and reduction with GFR. However, kidney disease in DM can occur without proteinuria in 13% of patients with DM and kidney disease.[15] Hence, screening for kidney disease should include serum creatinine and creatinine-based GFR estimation in addition to urine protein. Other risk factors that are often present hypertension, dyslipidemia, smoking, excessive salt intake, obesity needs to be targeted for effective CKD prevention. Angiotensin-converting-enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) have been shown to be useful in proteinuria kidney disease and to some extent useful in nonproteinuric kidney disease. In most patients, the ACEI or ARB can be continued **(Table 1)** if the GFR decline over 4 months after ACEI/ARB is less than 30% from baseline value and the serum potassium is less than or equal to

TABLE 1 | Recommended intervals for monitoring blood pressure, GFR and serum potassium for side effects ACEI or ARB in CKD[16]

Baseline value	SBP (mm Hg)	≥ 120	< 120
	GFR (mL/min/1.73 m^2)	≥ 60	< 60
	Early GFR Decline (%)	< 15	≥ 15
	Serum potassium (mEq/L)	≤ 45	> 4.5
Interval	After initiation or increase in dose of ACE inhibitor or ARB	4–12 weeks	≤ 4 weeks
	After blood pressure is at goal and dose is stable	6–12 months	1–6 months

5.5 mEq/L.[16] Care should be exercised in using a combination of ACEI and ARB especially in elderly as it has been shown to be harmful when given in combination. Further trials needs to confirm this finding as the trial findings are from a post-hoc analysis. ACEI and ARB also should be stopped temporarily during episodes of severe dehydration, hypotension and sepsis to avoid an episode of acute renal failure.[17]

To emphasis the importance of proteinuria in a patient with reduced GFR, modification of the existing CKD staging **(Figure 1)** has been proposed. Recent epidemiological evidence indicates that proteinuria patients with minimal changes in estimated eGFR may have greater risk for progressive loss of renal function than patients with more advanced reductions in eGFR who have little or no proteinuria.[18]

The existing national health program target infectious diseases, mother and child health, mental health and cancer. National programs and policies for noncommunicable disease (NCD) like CKD need national policies in sectors other than health. Influencing public policies in sectors like trade, taxation, education, agriculture, urban development, food and pharmaceutical production can readily achieve health gains than by making changes in national health policy alone with regard to NCD. Social determinants of NCD should be targeted with particular reference to the following: health in early childhood, the health of the urban poor, fair financing and equitable access to primary health care services. The main shared modifiable risk factors for NCDs (CVD, DM, hypertension, CKD and chronic respiratory disease) are tobacco use, unhealthy diets, physical inactivity and harmful use of alcohol. These should be addressed in common. In India, legislation banning tobacco use in public is in force and methods to warn and discourage sales are in place. Reducing salt levels in daily diet and in ready to eat food, eliminating industrially produced trans-fatty acids, decreasing saturated fats, limiting free sugars are urgently needed in India. Apart from legislation, the manufacturers are to be taken in confidence in reducing the level of these harmful substances. Introducing transport policies that promote active and safe methods of traveling to and from schools and workplaces, by walking or cycling; improving sports, recreation and leisure facilities; increasing the number of safe

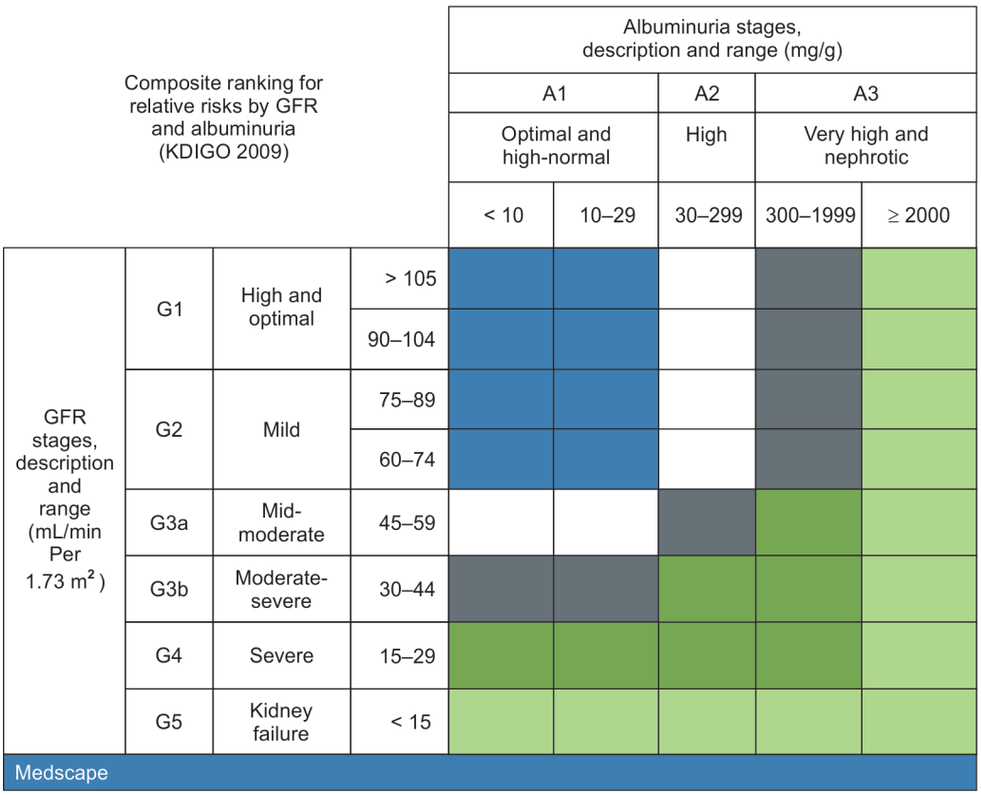

Figure 1: Composite ranking for relative risks by GFR and albuminuria from Kidney Disease: Improving Global Outcomes (KDIGO) controversies conference report[19]

spaces available for active play, will contribute to reduction in CKD and other communicable disease.[20]

Research for the prevention and control of NCDs needs to be promoted. The Indian Council of Medical Research (ICMR) has rightly identified DM, hypertension as thrust areas for research.[21] More needs to be done in the form of a national policy for NCD. The existing National Rural Health Mission[22] deals with DM and hypertension in the community, but more emphasis is been dedicated to mother and child health and communicable disease than NCD and there is no specific mention on CKD. However, management of the risk factors for CKD, i.e. DM and hypertension will indirectly cause some control on the CKD incidence.

CHALLENGES IN CHRONIC KIDNEY DISEASE MANAGEMENT IN INDIA

The average global prevalence values for treated ESRD (not diagnosed ESRD), dialysis and transplant patients were 280, 215 and 65 patients per million (ppm), respectively. In India, the average prevalence values for treated ESRD (not diagnosed ESRD); dialysis and transplant patients were 70, 60 and 10 ppm, respectively. This number is increasing globally at a rate of 7% every year.[4] It is estimated that only 10–20% of ESRD patients in India continue long-term RRT. It is estimated that in India in 1 year, there are 3,500 new renal transplant + 3,000 new continuous ambulatory peritoneal dialysis (CAPD) initiation + 15,000 new maintenance hemodialysis (MHD) patients.[23]

RENAL REPLACEMENT THERAPY FACILITIES

For the treatment of any disease, availability and affordability are two important issues. There is lack of adequate number of nephrologists (currently ≈ 1,000), hemodialysis (HD) units and the cost of treatment makes the treatment inaccessible for most. There is also unequal distribution in the availability of the nephrology services with only 9% and 2.5% of the nephrologist in the East and Central India, respectively.[23] There is rapid expansion of the MHD facilities mainly in the private sector in the last few years owing to growing need and increasing affordability of the people. The health cost of treating a patient on HD (dialysis + erythropoietin + medications) in India is around Rupees 9,000–10,000 per month in subsidized dialysis units and between ₹ 20,000 and 30,000 in private hospitals in the metros. However, the need far outstrips the availability. In the South Indian states, government sponsored programs like Rajiv Arogyasri[24] in Andhra Pradesh (AP) and Chief Ministers' Health Insurance Scheme[25] in Tamil Nadu (TN) provide for free dialysis and transplantation for the poor. The government pays the private hospitals via a health insurance company. However, the only way equity of therapy, accessibility and cost can come down in the long run is by improving the infrastructure in the government hospitals. Few nongovernment organizations (NGOs) like the Tanker Foundation in TN and Kerala offer subsidized treatment for the poor.

The majority of India lives in small towns and villages while most of the MHD facilities are in the cities. A lot of patients travel long distances to reach a MHD facility. Money and time is lost thereby. CAPD is a home-based therapy and is available even in remote places of the country. Around 7,000 prevalent CAPD patients are present at present in India. The cost is lesser compared to MHD and can be brought down further if more patients take on to CAPD. MHD is the major form of RRT in the world except in Mexico, Thailand and Hong Kong where CAPD utilization is high.[26] Despite the relatively few contraindications and the added advantage of it being a simple home therapy, the penetration of CAPD has been only 18–20% yearly in India. In Thailand with CAPD first initiative, there has been an exponential increase in CAPD penetrance.

In developing countries in Asia, CAPD offers certain clear advantages over HD such as simplicity, reduced need for trained technicians and nurses, minimal technical support requirement, lack of electricity dependence, online water purification and home-based therapy with institutional independence which has potential cost savings. Containing cost and promoting peritoneal dialysis (PD) is possible only through government support and health care insurance as shown by the example of the Thailand, Mexico and Hong Kong experience. This harsh reality with hardly any insurance coverage for Indian PD patients precludes the growth and expansion of PD programs. A growing number of MHD patients are currently affording HD in TN and AP mainly due to governmental support. Similar support for CAPD will reduce the cost of therapy for the government.

The "once-in-a-lifetime payment" scheme for patients paid to the manufacturing industry for PD supplies enabled the expansion of the PD program in India since 2003.[27] The lifetime scheme currently costs ₹ 700,000 payable as a single payment or three installments over a period of 3 years. Peritoneal dialysis *Suraksha* insurance for peritonitis, introduced in 2010 by a medical insurance company covers for everything that a patient needs during an episode of peritonitis.

In a survey of 275 South Asian nephrologists to assess roadblocks for CAPD expansion, the issues perceived by the nephrologists were peritonitis—30%, catheter-related problems—10%, lack of timely CKD education—91%, the lack of infrastructure and inadequacies of functioning HD unit—42% and the lack of extended care facility support—28%. Reluctance of insurance companies to reimburse CAPD concerned 74% of the physicians.[28]

RENAL TRANSPLANTATION

Contrary to general perception, the long-term cost of RT in lower compared to HD or CAPD.[29] The quality of life[30] and survival[31] are better amongst renal transplantation (RT) recipients. Yet, the RT rate in India is a paltry 3.25 per million per year.[32] The RT centers are concentrated in major cities and wide disparity exists in different regions of the country. Compared to cities, the awareness and affordability is lower in most regions of the country. Apart from money, availability of live related donor is a major cause for the ever increasing gap between the patients awaiting a RT and the patients who get a RT.[33,34]

India has approximately 180–200 RT centers with the most in the private sector. Annually, 3,500 transplants are done. Live related RT is more popular in India; a section of them is unrelated which is unethical and illegal in India. This is largely due to the gap between demand and availability that is unmet. Deceased donor transplant (DDT) can bridge this gap to some extent and can reduce the waiting time for RT and reduces commercial transplantation which is illegal in India.

In Spain and Portugal, the DDT rate is more than 30 donors per million population. In India, the deceased or cadaver RT rate in one of the better performing regions (TN, Gujarat, Maharashtra) in India is only 0.08 per million per year, i.e. 2% of the total transplantation. In India, 133,938 peoples have died of road traffic accidents in 2010[35] and of that 70% are brain dead. DDT has a great potential to bridge the ever widening gap between availability and demand of organs for transplantation. DDT involves declaring brain death, seeking permission from the relatives, retrieval of the organs, storage of organs, transport to the recipient's hospital and ultimately transplantation. Lack of awareness of brain-death concept, lack of organ donation awareness, perception of increased cost and mortality on RT, low number of RT centers performing DDT, lack of nationwide organ sharing network (NOSN) and lack of adequate infrastructure in the government are barriers for successful implementation of DDT.

TAMIL NADU MODEL OF DECEASED DONOR TRANSPLANTATION

The role of grief counselor cum transplant coordinator was realized and a transplant coordinator is appointed and is made available round the clock to coordinate all aspects of transplantation in the hospitals. The hospitals are required to upload the details of the transplantation on the government web site (www.tnos.org). Each hospital maintains a waiting list of patients awaiting transplantation that is frequently updated. In the absence of a NOSN, the TN model involves allocation of one kidney, liver and heart automatically to the hospital where the deceased donor organs are harvested. The second kidney, the liver and the heart (if the hospital where harvesting has taken place only does renal transplantation) will be allocated to patients in other hospitals by the convener. The postmortem of the brain dead cadaver donor is performed in the premises of the organ retrieval hospital to save time and worry for the donor family. A full recipient report is sent to the central convener of the transplant program within 48 hours of discharge of the recipient and uploaded to the website http://dmrhs.org. A transplant advisory committee involving members of the health ministry, NGOs, private and government medical college hospitals in the state, monitor the functioning of the program. The combined effort has resulted in the harvesting of 223 deceased donors in the state of TN during the period October 2008 to December 2012.[11]

GOVERNMENT SUPPORT FOR RENAL TRANSPLANTATION

For good in the Eleventh Five Year Plan the health spending is increased to 2% of gross domestic product (GDP).[36] In some of the Southern States, the government actively oversees the running of the transplant program, lays the policies for organ allocation and sharing of organs between government and private hospitals. The government offers the transplant medicines free of cost lifelong. This has reduced the commercial RT considerably. The Union Health Ministry is in the process of setting up the autonomous National Organ Procurement and Distribution Organization (NOPDO) at the Center and 10 State Organ Procurement and Distribution Organization (SOPDO) for the National Organ Transplant Program (NOTP). The organization will strive to increase the availability of organs from cadaver donors, improve the infrastructure for organ retrieval and offer post-transplant services to recipients. They also intend to bring the public and private hospitals under the program as the majority of the transplantation services are available with the private sector.[37] The NGOs have been doing a great job not just in promoting awareness of organ donation but have been instrumental in initiating policy change by the government and in aiding the government in organizing a regional network. NGOs in partnership with the governments have been successfully promoting and helping to implement the deceased donor program. The FORTE (Foundation for Organ Transplantation and Education), Bangalore; MOHAN (Multi Organ Harvesting Aid Network), Chennai and Hyderabad; Narmada Kidney Foundation, ZTCC (Zonal Transplant Coordinating Committee), Mumbai; ORBO (Organ Retrieval Banking Organization), New Delhi; DONATE (Delhi Organ Procurement Network and Transplant Education), Delhi—are some of the active groups.

CONCLUSION

Early detecting of CKD by screening for kidney disease in high-risk patients, early referral to nephrologist, appropriate treatment of hypertension, DM and other risk factors, lifestyle modification with specific emphasis on reduction in salt intake, physical exercise, abstinence from smoking, will retard progression of kidney disease to an advanced stage. There is an urgent need for a national program to control the epidemic of NCDs like hypertension, DM, chronic respiratory and CKD in India. The current dependence on the private sector for treatment of kidney patients with severe renal disease needs to be reduced with infrastructure upgradation in government run hospitals to facilitate accessibility of treatment for the majority of our population who cannot afford treatment in private hospitals. Till the country is able to provide universal health coverage, state sponsored health insurance schemes like the ones in TN and AP can make the RRT affordable for the poor. DDT program should be given impetus to compliment the live related RT program to reduce the commercial transplantation and make transplantation affordable to all.

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