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**KIDNEY DISEASE IN THE NORTH CENTRAL PROVINCE OF SRI LANKA:
BEYOND THE AETIOLOGY**

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An apparently new form of chronic kidney disease (CKD), mainly affecting rural and underprivileged paddy farmers, has been identified in the North Central dry zone of Sri Lanka⁽¹⁾. At present the cause remains controversial and subject to debate. The disease remains labelled as Chronic Kidney Disease of Uncertain aetiology (CKDu)⁽²⁾. CKD is recognized as the major public health problem in the North Central province of Sri Lanka⁽¹⁾.

Since 2012 I have served as the consultant nephrologist at Teaching Hospital Anuradhapura. To date, I am the nephrologist with the longest full time service in the North Central province. I state this merely to put my talk in perspective, and not to place myself on par with several other nephrologists who have done much greater service in the region. I have witnessed and experienced numerous challenges in providing quality care to CKD patients in the region. These challenges include screening practices, patient management issues and ethical dilemmas. Devastating socio economic problems limit patients' ability to seek and continue treatment. Lack of population awareness has led to many

problems, including vulnerability to exploitation.

I have played a role, with numerous others, in trying to address and overcome these problems. A national guideline for management of CKD and CKDu has been published under the co authorship of my colleague and I⁽³⁾. Steps have been taken to provide protocol based kidney care in the region. Technical problems have been overcome, to increase the provision of haemodialysis by 500% in my unit. Satellite dialysis has been set up. New renal replacement modalities have been established. Our ongoing community screening and awareness programme is complementary to the official programme, and more comprehensive. This has provided insights for the new national guideline for community screening of CKD, to which I am a contributor⁽⁴⁾. Through the Anuradhapura Kidney Protection foundation, many patients have received financial assistance and social support. Our research activities have addressed relevant issues. They have been presented locally and overseas, and won awards.

Great interest is being shown in identifying the cause of CKDu. While this is of utmost importance, wider awareness is needed regarding other challenges. This story is about successes, failures, limitations and requirements in addressing these. My message is on behalf of a disadvantaged section of our population, with little bargaining power, reaping the bitter harvest of a man made epidemic.

The medical profession needs to play a multifaceted role in addressing the CKDu problem. A major contribution is needed to identify and eliminate the cause or causes. It is also necessary to look beyond the aetiology. Quality healthcare must be provided. Sustainable strategies to assure quality of care must be implemented. Quality healthcare must be accessible, and should not place an undue burden on patients. Education of patients and at risk populations is needed, not only to promote prevention and compliance, but also to empower them to resist exploitation. Ideally, CKDu should be prevented. Failing this, the CKDu patient should be detected early, be offered standard care irrespective of where he or she is detected, have justifiable access to all treatment options, and not face undue financial, social or other burdens due to the disease or treatment.

I have been the consultant nephrologist at Anuradhapura for four years. My experiences have left me with the firm belief that the situation is improvable. A coordinated effort is needed by the medical profession. The first step is to initiate a constructive dialogue regarding problems, initiatives, successes, failures, limitations, and requirements. I

share my experiences in the hope of making a contribution towards this.

The obvious and decisive solution to the CKDu problem is to identify and eliminate the cause or causes. My involvement in this aspect has been minimal. However, CKD, in general, is increasingly recognized as a “multi hit” condition ⁽⁵⁾. Surprisingly, poverty and malnutrition have been largely overlooked as contributing factors for CKDu. Worldwide, disadvantaged communities have an increased CKD burden. Such communities include not only farming populations. People in low resource settings, racial and ethnic minorities, indigenous populations and other socially disadvantaged communities have been affected. In fact, “embryonic origins of kidney disease in later life” was the topic of a keynote address at the International Society of Nephrology Sessions 2015 ⁽⁶⁾. Low birth weight, due primarily to nutritional factors, is associated with kidney disease ⁽⁷⁾. Low birth weight also predisposes to more rapid progression of renal disease in later life ⁽⁸⁾. In poorer communities, maternal malnutrition is likely to be a significant, independent risk factor for low birth weight ⁽⁹⁾. Maternal protein restriction impedes kidney development in rats ⁽¹⁰⁾ even though birthweight is not affected ⁽¹¹⁾. We have found that a majority of CKD patients attending clinic at Anuradhapura has protein energy malnutrition ⁽¹²⁾. We have also found that kidney sizes, in healthy subjects, in a rural farming village in Anuradhapura, are smaller than accepted values ⁽¹³⁾. A second hit may lead to renal disease in low birth weight persons. The second hit may be a nephrotoxin⁽¹⁴⁾. Malnutrition may therefore tie in with the postulated toxic aetiologies for

CKDu. Maternal nutritional supplementation improves nephron numbers in animal models⁽¹⁵⁾. In humans, balanced protein energy supplementation during gestation was associated with an increase in the mean birth weight⁽¹⁶⁾. Better studies are needed to investigate malnutrition in the region, and a possible link to CKDu. Prevention of malnutrition is a relatively risk free intervention⁽¹⁶⁾. Alleviation of poverty has numerous advantages in any case. These strategies should be actively pursued, pending studies, and considered priorities for funding. Much interest is shown in finding the cause of the kidney disease affecting poor farmers. It should also be recognized that their poverty itself may be a cause.

Early detection is a cornerstone of CKDu management. CKD is typically silent until later stages⁽¹⁷⁾. Therefore, early detection requires screening of asymptomatic subjects in endemic areas. CKDu was initially described using dipstick measurement of albuminuria⁽¹⁸⁾. Since then, dipstick albuminuria was the tool for population screening. However, guidelines state that using both urinalysis and serum creatinine estimation is mandatory for screening of CKD⁽¹⁹⁾.

The Anuradhapura renal unit conducted a stall at the Oyamaduwa “Dayata Kirula” exhibition in 2011. Screening with both urinalysis and serum creatinine estimation was offered. Results strengthened suspicions that dipstick albuminuria was an inadequate screening tool. Therefore, in 2012, the renal unit launched its own screening and awareness programme. This was complimentary to the official community

screening programme, but more comprehensive. The provincial director of health kindly gave permission and provided transport. We raised funds through the Anuradhapura Kidney Protection Foundation, a registered charity. To date, we have screened over 14,000 subjects. Both urinalysis and serum creatinine were tested. Interestingly, but perhaps not surprisingly, our data showed that urinalysis alone will miss out over 30% of cases⁽²⁰⁾. A new national guideline has now been published for community screening⁽⁵⁾. This recommends using both urinalysis and serum creatinine. Testing for serum creatinine is now being practiced. However, this is being opposed citing practical difficulties. A backward step at this juncture should be avoided. It is our recommendation that a consultant community physician, based in the affected area, should lead the screening programme. This should enhance practicality. Adequate resources should be provided.

Once detected, patients should be offered standard care, irrespective of how or where they were detected. CKD patients can be managed at primary care in most cases. However, specialist referral is needed when indicated⁽⁴⁾. Timely nephrology referral has been shown to improve outcomes⁽²¹⁾. High risk of kidney failure within one year is an indication for specialist referral⁽²²⁾. Certain health system characteristics are associated with late referrals⁽²³⁾. These include unavailability of formal guidelines, lack of referring physicians’ knowledge, lack of organized means of communication between referring physicians and nephrologists, mainly at tertiary care hospitals.

Only 32% of our patients had been under a nephrologist's care for one year before starting dialysis. In contrast, 48% had been seen within one month of starting dialysis ⁽²⁴⁾.

Health system characteristics that are known to be associated with late referrals, may also contribute to poor management. These need to be addressed. Progress has been made with formal guidelines. Upon taking up duties in Anuradhapura, I wrote and circulated a guideline to be used in this district. This was later used in several other districts. The Epidemiology Unit, Ministry of Health approached me to publish these as a national guideline. After expert reviews and updates, a national guideline has been published. This is under my authorship and my colleague has contributed a chapter on CKDu ⁽⁴⁾.

Lack of referring physician knowledge may also contribute to suboptimal management, in addition to delayed referrals. In our experience, this issue is highly variable, complicated and sensitive. It must be stated that the majority of junior doctors in the region are knowledgeable and efficient. Yet we do see problems. In addition to delayed referrals, we see liberal and indiscriminate use of non-steroidal anti-inflammatory drugs. In an era when CKD is thought to be a "multi hit" condition ⁽⁶⁾, this is extremely worrying. Poor blood pressure control, drug errors and poor monitoring of renal functions are other areas showing major deficiencies. Unnecessary dietary restrictions cause additional problems in a population with a high prevalence of malnutrition. In order to improve communication and knowledge, our unit established a renal helpline and an e-mail. They were not utilized and fell into disuse.

We also conducted a symposium on diet in renal disease which was poorly attended ⁽²⁵⁾. We have designed flow charts to be used at various stages of CKD. These have been compiled and distributed to hospitals in the region. Deficiencies in CKD management in primary care have been seen elsewhere in the world. Audit based education may improve performance ⁽²⁶⁾. Designing such a programme may not only help to address problem areas, but also to appreciate and motivate units and individuals performing beyond expectations. Special mention should be made of some hospitals, which have established protocol based renal clinics. This is a positive step, in a region where travelling costs and commitments present a major barrier to seeking treatment. Not only is travelling costly and time consuming, but early and late travel is dangerous in some areas, due to threats from wild elephants. Protocol based care at local hospitals and avoiding unnecessary referrals, is an attractive and a low cost option. I have visited a number of hospitals to initiate such protocol based renal clinics. The major barrier appears to be lack of resources. Most small hospitals are unable even to access basic investigations such as haemoglobin level and serum electrolytes. Developing services at these hospitals should be a priority. Measures to restrict or rationalize the use of non-steroidal anti-inflammatory medications may also be something to look at. Contrary to popular belief, the vast majority of CKDu patients do not need dialysis or transplantation. However, development of facilities seems to target renal replacement. Facilities to treat CKD patients at smaller hospitals remain minimal.

Providing quality care in the region depends on high standards being maintained at the referral centre. Our unit at Teaching Hospital Anuradhapura is the main referral centre for Anuradhapura district and some other areas. Self-audits at our clinics revealed multiple deficiencies. Concordance with recommendations for monitoring and counselling ⁽¹⁹⁾ was found to be poor. Immunization prior to renal replacement therapy and referrals for vascular access creation were not happening in a timely manner. A detailed plan was developed to improve care at our clinics, without additional inconveniences to patients. Patients were categorized and clinics were restructured. This facilitated appropriate health education, specialist involvement and optimization of clinic numbers. A colour coding system and protocols were devised for each clinic. The renal clinics at Medawachchiya, Kebithigollawa and Padaviya, which are supervised by the consultant nephrologist at Anuradhapura, were restructured in a similar manner. Rolling audits need to be established to ensure continuation of quality care.

Renal replacement, in the form of dialysis or transplant, is the preferred option for a majority of patients in end stage kidney disease. This holds a number of challenges. These involve medical, technical, ethical, financial and social issues.

At the time I assumed duties, only eight dialysis machines were functioning, and only about half of them were working at any given time. The functioning machines could not deliver uninterrupted dialysis due to poor reverse osmosis water supply. Patients had to

wait in queue for up to 24 hours to get a dialysis slot ⁽²⁷⁾. A series of meetings and discussions was initiated to improve the situation ⁽²⁸⁾. Representatives from service providing companies were summoned for the meetings. Experts from the water board kindly attended to provide expert advice, and performed water testing. An additional water treatment plant and a pre-treatment plant were installed. Most technical problems have now been addressed. Provision of dialysis has increased by 500%, with 25 fully functional dialysis machines ⁽²⁹⁾.

It has been stated that the priority short-term option to help ESRD patients is to install dialysis services rapidly throughout the affected areas. While whole heartedly agreeing with this statement, I would also like to add that dialysis should be designed to provide meaningful outcomes. Do we want a patient who is well dialysed, has a reasonable quality of life, survives on dialysis for a reasonable length of time, and makes a contribution to his family and society? Or do we want a patient who is dialysed, but having a very poor quality of life unable to even perform self-care activities, has a high symptom burden, does not survive on dialysis for very long, is a massive financial burden on his family, but looks good as a statistic? i.e we are providing free dialysis to this number of patients. The answer, to a mainly medical audience, is obvious. But what really happens? Achieving dialysis targets with stretched resources remains a challenge. In spite of the fivefold increase in dialysis provision, the number of dialysis nurses remains the same. We found that known one year survival in our haemodialysis patients is dismal, at 29%. To the best of our knowledge,

ours is the only study of mortality rates on haemodialysis in Sri Lanka⁽³⁰⁾. Chronic fluid overload is a killer. Most dialysis patients depend on ultra-filtration on dialysis for fluid removal. Both chronic fluid overload and too rapid ultra-filtration are harmful. Sixty per cent of our patients needed ultra-filtration rates in excess of recommendations. We have had to improvise, combining acute peritoneal dialysis sessions with haemodialysis. Our work was presented internationally⁽³¹⁾. A unit protocol for haemodialysis quality assurance was designed, in order to deliver target oriented dialysis⁽³²⁾. A rolling audit was planned. This is seriously hampered by staff shortage and shortage of dialysis slots. It should be emphasized that provision of equipment should be balanced with adequate staffing.

Seventy four percent of our clinic patients are at or near stage 5 CKD⁽²²⁾. Current dialysis facilities are able to accommodate only a maximum of about 175 patients at standard recommendations⁽³³⁾, although we stretch our resources to accommodate more. This raises ethical issues regarding allocation of a limited resource. Benefiting people equally entails providing equal chances at a scarce intervention, rather than equal amounts of it⁽³⁴⁾. Absence of transparent policies for dialysis allocation remains a frustrating problem. Concerns have been raised about gross inequalities in access to dialysis services in the country⁽³⁵⁾. Patients are also vulnerable to exploitation. A transparent and fair national policy for dialysis allocation is an urgent need. Patients who stand to gain maximum benefit should receive dialysis. Known key predictors of survival on dialysis, such as age, co morbidities, functional status

and nutritional status should be considered. Pending a national policy for dialysis allocation, it seems reasonable to request individual units to formulate their allocation policies. These should be clearly and publicly stated, and adhered to as far as possible.

Transplantation⁽³⁶⁾ and chronic ambulatory peritoneal dialysis have now been started at Anuradhapura. We performed the first kidney transplant at District General Hospital Polonnaruwa earlier this week. This was the first kidney transplant to be done in a district general hospital in Sri Lanka. Development of renal replacement services in the region is a great convenience to patients. All renal replacement facilities are free of charge. The Anuradhapura Kidney Protection foundation provides Rs. 25,000 to every transplanted patient.

CKD of uncertain aetiology affects low socioeconomic groups⁽³⁷⁾. Dialysis patients, in particular, face devastating socioeconomic problems. Haemodialysis patients at our unit, have an average household income of Rs. 14777. Additional costs per dialysis session were Rs. 880.96, in spite of the treatment being free of charge. This included travelling costs for patients and carers, and costs for meals from outside. Sixty eight percent were unemployed in spite of reasonable education levels, and only 4.3% were in skilled occupations⁽³⁸⁾. Better social support is essential to obtain meaningful benefits from the expensive treatment they receive. Time commitment per dialysis session was 11 hours⁽³⁸⁾. Travelling time of more than one hour is associated with a 20% increased mortality

compared to those who travel fifteen minutes or less ⁽³⁹⁾.

The Anuradhapura Kidney Protection Foundation and other donors have tried to help. Scholarships are awarded to many children of dialysis patients. Meals are provided to patients and relatives while at hospital. Vocational training has been arranged for patients and families. One patient has completed a course at the ornamental fish breeding and training centre at Rambadagalla. The National Apprenticeship board has organized lectures and offered vocational training. Several patients have received financial assistance for self-employment. Unfortunately, these efforts have failed to make any notable difference. Most patients find it difficult to meet travelling and other costs to attend regular dialysis. The government needs to intervene, and provide subsidized or free travelling to obtain medical care. Dialysis patients need to attend hospital frequently and regularly. Ideally, at least two vehicles should be provided to the hospital to transport dialysis patients to their nearest town. This will reduce travelling time commitment as well as the cost. This is the practice in settings like the National Health Service of the United Kingdom. The hospital is responsible for dialysis patient transport. On the long term, satellite dialysis centers are the ideal solution. Travelling costs and time commitments should not stop dialysis patients from leading a productive life. Dialysis treatment should not impose devastating financial strains on their families.

However, while ardently advocating support for renal patients, I would warn against

creating a “helpless kidney patient” mentality, where patients expect the government and donors to look after all aspects of their lives. Many of my patients, including some on dialysis, lead active and productive lives. It would be best if patients are encouraged and supported to help themselves.

Conservative care is an accepted form of treatment in end stage kidney disease. This may be appropriate for some, while others may not receive renal replacement due to resource limitation or financial constraints. A standard conservative care programme is lacking. Conservatively managed patients at Anuradhapura have a high symptom burden⁽⁴⁰⁾. Conservative management should be supported by a comprehensive management programme that is able to deliver advance care planning, coordinated end of life care, protocols for symptom and pain management, psychological care, spiritual care, and culturally sensitive care for the dying patient and their family ⁽¹⁹⁾. Home based care is ideal, but not practical, in our setting. The next best option is the closest medical institution. However, most referrals for local hospital care were coming back to us, for little or no reason. A new referral format for shared care, with instructions and options for communication, is being used ⁽⁴¹⁾. The situation with back referrals has improved to some extent. We also conducted a certificate course in palliative care for renal nurses ⁽⁴²⁾. This was well attended by nurses from all parts of the country. Unavailability of medications used in conservatively managed advanced CKD patients, is a limiting factor for symptom control. We have informed authorities regarding required medications ⁽⁴³⁾, and await a response.

Raising community awareness and education may have beneficial effects not only on prevention and compliance, but also to empower people in affected areas to resist exploitation. It is also necessary to alleviate fear of kidney disease, which is frequently disproportional, and counterproductive. I have experienced an incident where a patient's brother collapsed, and needed cardiopulmonary resuscitation, upon being told that his sister had kidney disease. Our fortnightly screening programmes in rural villages include a 30 minute educational discussion, led by the consultant nephrologist. These discussions focus on prevention, early detection and treatment of kidney disease. We carried out a survey of current beliefs and conceptions related to kidney disease in rural farming populations in the region ⁽⁴⁴⁾. This will be useful in planning awareness programmes and messages. Alternative medical practices are being actively marketed in CKDu affected areas. One study and numerous media reports have described benefits of alternative medicine. We found no publications describing limitations of alternative medicine. Therefore, we presented a case series of patients returning to western medicine from alternative medicine ⁽⁴⁵⁾. The majority are now on renal replacement. While not attempting to undermine alternative medical practices in any way, limitations should also be known, to enable patients to make informed choices.

The role of the Anuradhapura kidney protection foundation in supporting kidney disease patients should be mentioned. This is a volunteer organization and a registered charity, complying with financial auditing regulations. It has supported our unit by

providing equipment and developing infrastructure. Ours is one of the few units to provide ambulatory blood pressure monitoring, donated by the above foundation. Our findings in renal patients have been presented ⁽⁴⁶⁾. The foundation has also assisted patients financially, including monetary assistance to transplant patients and self-employment assistance. Its website was launched at www.ckdcpf.org.

Researchers have shown comparatively less interest regarding management of CKDu and related issues. Our studies have been focused in this area, and presented locally and overseas. We won the first place for free papers at the Anuradhapura Clinical Society sessions, and the second place at the Kurunegala Clinical Society sessions, in 2014.

Addressing the kidney disease endemic in the North Central province goes beyond identifying and eliminating the cause. It should be remembered that a disadvantaged population is affected. Sustainable and adequate screening programmes need the support of specialist community physicians based in the region. Standard treatment needs to be delivered without undue travelling burdens on patients whenever possible. To this end, current endeavors to establish protocol based renal clinics in smaller hospitals need to be supported. Organized communication between nephrologists and non-specialists needs to be arranged, and audit based education should be implemented. Above all, financial constrains should not be a limiting factor in obtaining treatment. If free healthcare is to be meaningful, needy patients, especially those on dialysis, need

financial and social support. Lack of a transparent and fair policy for allocation of dialysis slots is a frustrating and embarrassing problem, and needs to be addressed without delay.

Providing quality care to CKD patients in the North Central province requires a coordinated effort. It is regrettable that none of the practicing consultant nephrologists in this province are part of any bodies or committees looking into this aspect.

CKDu may be a result of human activities affecting the environment. Hence, society has an additional responsibility. The disease affects poorer rural farmers, causing devastating socio economic problems in addition to medical problems. Understandably, the aetiology of this epidemic has triggered great interest. Identifying and eliminating the cause or causes of the epidemic is ideal. However, provision of quality care should not be neglected. Quality healthcare, without restrictions due to financial circumstances, should be provided to this disadvantaged population, whose treatment may be limited by factors such as travelling and financial difficulties and lack of transparent policies for justifiable allocation of resources. The medical community can play an important role to overcome this.

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