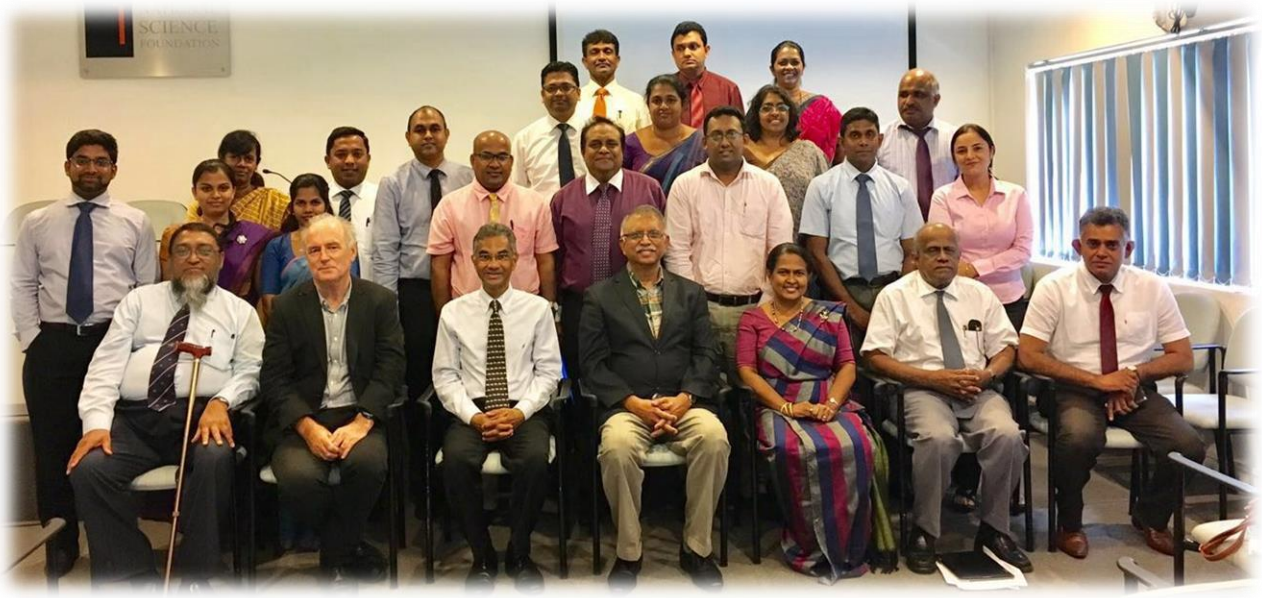
Workshop report

'Designing a step-wise approach to estimate the burden and to understand the etiology of CKDu in Sri Lanka'



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Executive summary

Background and rationale

Chronic kidney disease of unknown etiology (CKDu) is one of the most important public health problems in Sri Lanka affecting predominantly farmers. Based on existing data, select Divisional Secretariat Divisions of 11 districts in the country have been designated as 'high risk' for occurrence of CKDu. In April 2016, the World Health Organization (WHO) Country Office for Sri Lanka and Presidential Task Force jointly convened a three-day international expert consultation to develop consensus recommendations for addressing CKDu in Sri Lanka. Recommendations of the consultation included the need for a uniform case definition and community based surveillance to measure the burden and trends. In addition, the need for long term cohort studies to identify the risk factors was emphasized.

The National Science Foundation (NSF) and World Health Organization (WHO) Country Office for Sri Lanka jointly organized a two-day workshop on 24th and 25th October, 2016 to brainstorm and develop consensus among experts on case definition of CKDu to be used at various levels of the health system. A draft protocol for implementing community based surveillance was agreed upon. The design of resurveys and cohort studies based on the findings of the community based surveillance was also discussed. Participants comprised nephrologists, physicians, clinical researchers, non-medical researchers, epidemiologists, program managers at the national/province level and international experts.

Scientific sessions

The workshop objectives and expected outcomes were explained by the key officials from National Science Foundation, Ministry of Health, Nutrition and Indigenous Medicine and WHO Country Office for Sri Lanka. Morning session on day 1 included presentations on the existing sources of data and types of data available for CKDu. The gaps in the data for measuring the burden and trends were highlighted. This was followed by a presentation on the concept of public health surveillance and case definitions at three levels. Two protocols, an international and a national protocol on CKDu were also presented to set the stage. Participants were then divided into two groups. Day 1 group work was for developing consensus on the case definition. Day 2 group work focused on the development of protocol for the community based surveillance for CKDu. Both the groups made presentations followed by open discussions which led to a final consensus.

Outcomes of the meeting

- ***Consensus on the case definition of CKDu***: There was agreement on the three levels of case definition namely suspected, probable and confirmed CKDu**.** The participants agreed that the use of a uniform case definition at different levels of health system for the purpose of screening, surveillance and patient management will facilitate the understanding of the burden, geographical distribution and time trends of CKDu in Sri Lanka.

- ***Consensus on community based surveillance:*** The group agreed on the need for community based surveillance and also developed a draft protocol for implementation of this. The protocol involves cross-sectional surveys of one or more specific populations; each survey should be based on a particular geographical area, and the survey should then include all adults, or a random sample of adults, in this area. However, the protocol also includes provision to design cohort studies based on the results of the initial cross-sectional surveys.

Background

Chronic kidney disease of unknown etiology (CKDu) is one of the diseases of public health importance in Sri Lanka affecting predominantly farmers. Either all or few of the Divisional Secretariat Divisions of 11 districts (out of 25 districts) in the country (Anuradhapura, Pollonaruwa, Kurunegala, Ampara, Trincomalee, Badulla, Mullativu, Vavuniya, Matale, Monaragala and Hambantota) have been designated as 'high risk' for the occurrence of CKDu. The World Health Organization (WHO) Country Office for Sri Lanka and Presidential Task Force jointly convened a three-day international expert consultation in April, 2016 to develop consensus recommendations for addressing CKDu in Sri Lanka. The consultation provided the opportunity to review the existing systems of surveillance and registries for CKD/CKDu in Sri Lanka. The participants in the consultation noted that the data generated to date did not facilitate the estimation of the magnitude and distribution of the disease burden in the country since it was not based on random population-based samples. Furthermore, the sources of data were not designed to generate information to formulate hypotheses that could guide further research to identify the causes of CKDu. Several recommendations emerged from the consultation. One of the key recommendations was to develop a robust surveillance system to understand the burden, geographical distribution and time trends of CKDu in Sri Lanka. The surveillance system should provide a platform for long-term research to understand the role of potential risk factors and document the usefulness of ongoing interventions. Another recommendation was to develop a uniform case definition for CKDu at various levels of the health system.

To take forward the key recommendations on surveillance, the National Science Foundation (NSF) and World Health Organization (WHO) Country Office for Sri Lanka jointly organized a two-day workshop on 24th and 25th October, 2016. The workshop provided a platform to develop consensus among experts on the case definition of CKDu and the protocol for community based surveillance. Participants comprised nephrologists, physicians, clinical researchers, non-medical researchers, epidemiologists, program managers at the national/province level and international experts.

The objectives of the workshop were as follows:

- Develop consensus on a case definition for CKDu in Sri Lanka at three levels (suspected CKDu, probable CKDu and confirmed CKDu).
- Design a protocol for community-based surveillance to estimate the magnitude and distribution of the CKDu burden, with provision to design subsequent cohort studies to understand better the causes of this condition.
- Identify the pathways to improve data linkages between various existing databases and utilize the data to generate information for policy making.

Proceedings: Day 1

The workshop objectives and expected outcomes were explained by the key officials from National Science Foundation, Ministry of Health, Nutrition and Indigenous Medicine and WHO Country Office for Sri Lanka in the opening session of the workshop. Prof. Sirimali Fernando, Chairperson, National Science Foundation welcomed the participants. She explained that, despite two decades of research, there was lack of reliable information on burden and risk factors of CKDu. She emphasized the need to develop collaborative research projects to solve the mystery of CKDu. Dr. Sarath Amunugama, Deputy Director General of Public Health Services of the Ministry of Health, Nutrition and Indigenous Medicine explained the ongoing initiatives related to CKDu. He urged the participants to develop consensus on the various aspects of CKDu as envisaged in the workshop agenda. Dr. Jacob Kumaresan, WHO Representative for Sri Lanka highlighted the need for rigorous peer review throughout the research process to ensure quality and validity of the findings emerging from various studies that are being planned to answer various questions about CKDu.

The first session was on the current status of burden of CKDu in Sri Lanka. Dr. Paba Palihawadana, the Chief Epidemiologist of the Ministry of Health, Nutrition and Indigenous Medicine presented the epidemiology of chronic kidney disease based on the data collected from 50 sentinel hospital sites. The distinction of CKD versus CKDu was not evident from this data. There were 29662 patients registered between 2010 and December, 2015. In addition, 3820 cases were registered between January to September, 2016.

Prof. Rezvi Sheriff, Research Fellow, National Science Foundation, presented the existing sources of data and types of data available for CKDu. The gaps in the data for measuring the burden and trends were highlighted. Routine morbidity and mortality surveillance through hospital statistics and vital registration systems did not have a specific category for CKD or CKDu. Community based screening programme in areas designated as 'high risk' had challenges of low coverage and lack of exposure data. The special household survey that has been conducted in the designated 'high risk' areas in 2015, collected information only on the diagnosed CKD/CKDu patients and did not include a method to identify the early asymptomatic cases, precluding the use of the data to estimate the population prevalence of CKD/CKDu. Data on CKD patients in the Provincial Renal Disease Prevention and Research (PRDPR) Unit was restricted to the North central Province of the country. Though this database was derived from household data and included some exposure data, the period of data collection ranged from 2003 to date with no updating to exclude deaths. National Renal register maintained by the Epidemiology unit only recorded diagnosed cases and no data was available on denominators. The renal registry maintained by the Sri Lanka Society of Nephrologists was restricted to patients on dialysis.

In the second session, Dr. Prabhdeep Kaur, Epidemiologist, National Institute of Epidemiology, Chennai presented the key concepts and attributes of surveillance system for chronic diseases. She clarified the differences between case definitions for surveillance versus case management. Various examples of existing surveillance systems for various communicable and non-communicable diseases were described. Dr. Eranga Wijewickrama, Senior Lecturer, Dept. of Clinical Medicine, Faculty Medicine, University of Colombo presented a protocol for national level survey for prevalence of Chronic Kidney Disease. This survey will cover all the districts and will be carried out along with a national survey on prevalence and risk factors for diabetes. Prof. Neil Pearce, Head of the Department of Medical Statistics and Professor of Epidemiology and Biostatistics, London School of Hygiene and Tropical Medicine presented an international multicentric protocol on estimating eGFR at the community level. This is known as the Disadvantaged population eGFR Epidemiology study (DEGREE), and is being conducted or planned in a number of different countries. It involves a community-based survey in a defined geographical area; within each study area, either all adults will be studied, or a random sample of adults, with a minimum sample size of 1000. The study will be conducted in multiple sites around the world. The initial survey will provide important information in itself, and will also provide an opportunity to develop cohort studies in these populations.

Participants were then divided into two groups. First group work aimed to develop consensus on the case definition. The three levels of case definition suspected, probable and confirmed CKDu were discussed. The suspect case definition can be used at the field level or facilities with the lack of nephrologist. The probable case should be defined by trained physician or nephrologist after thorough clinical and laboratory evaluation. The confirmed case will be defined only based on the histopathological examination.

At the end of the group work, both the groups made presentations followed by open discussions which led to final consensus on the three levels of case definition suspected, probable and confirmed CKDu to be used at different levels of health system for the purposes of screening, surveillance and patient management (Annexure I). The formats used for the offline information generation of the sentinel surveillance of CKD/CKDu, existing community based screening programme and community surveys in the areas designated as 'high risk' need to be revised to accommodate the use of the case definition (Annexure II).

Proceedings: Day 2

Day 2 group work focused on the development of protocol for CKDu. The groups discussed the objectives of surveillance. The key objectives included estimation of the distribution of the eGFR in the selected geographical locations, estimation of the proportion with eGFR less than 60ml/min or albuminuria and proportion with suspected CKDu. The groups discussed the detailed methods for the surveillance including study sites, study population, inclusion/exclusion criteria, sample size, sampling strategy, data collection tools and implementation plan etc. The need for quality assurance for data collection and laboratory measurements was also emphasized. Development of cohorts in the select surveyed population based on the findings of the community based surveillance was also discussed and agreed upon.

Group work was followed by presentation by both groups. An open discussion after the presentations provided opportunity to brainstorm key components of the protocol. The group reached consensus regarding the objectives and key methods for the surveillance protocol (Annexure III) and the design of the cohort study (Annexure IV)

The next session aimed at identifying the pathways to improve data linkages between various existing databases and included presentations on the online database for the CKD patients maintained by the Epidemiology unit of Ministry of Health and the online database for dialysis patients maintained by Sri Lanka Society of Nephrology. Presentations were followed by the open discussion. The need for a single consolidated database was emphasized. A small group of experts could explore the ways of synthesizing the data from two databases. The data can be converted into information that will be useful for policy making.

The key officials from the National Science Foundation and WHO Country Office Sri Lanka summarized the proceedings of the meeting and the way forward to implement the case definition and the community based surveillance protocol in the near future.

Outcomes and Recommendations

- ***Consensus on the case definition of CKDu***: There was agreement on the three levels of case definition namely suspected, probable and confirmed CKDu**.** The participants agreed to use the case definition developed by consensus at different levels of health system for the purpose of screening, surveillance and patient management to facilitate the understanding of the burden, geographical distribution and time trends of CKDu in Sri Lanka. The case definition should be published and disseminated to all the relevant authorities.

- ***Consensus on community based surveillance:*** The group agreed on the need for community based surveillance and also developed a draft protocol to be implemented; this is based on the international protocol for the DEGREE study, so that the findings from Sri Lanka can be compared with those in other countries.

- ***Develop cohorts to identify the risk factors for CKDu:*** Baseline information from the community based surveillance will be used as the platform for developing cohorts to study the risk factors.

- ***Analyze and interpret the available data from various sources:*** A single consolidated database needs to be formulated using the two existing renal registries. A small group of experts may explore the ways of synthesizing the data from two databases. The data can be converted into information that will be useful for policy making. The key indicators should be developed and be reported periodically, with results disseminated to various stakeholders and made available in the public domain.

Annex I: Case definition of Chronic Kidney Disease of unknown etiology (CKDu)

Three levels of case definition are as below:

Suspected CKDu

- Essential criteria: eGFR < 60 mL/min using CKD EPI equation: One time measurement using standardized methods for creatinine measurement **OR** albuminuria > = 30 mg/g

  <u>Exclusion criteria to identify suspect CKDu among those satisfying above criteria</u>

  i. Urine protein: creatinine ratio > 2 g/g creatinine **OR** urine albumin: creatinine ratio >0.3 g/g creatinine
  ii. Hypertensives on treatment with more than two drugs **OR** untreated blood pressure of more than 160/100 mmHg (preferably using electronic BP apparatus, sitting position, at least two readings one minute apart)
  iii. History of diabetes **OR** being on treatment **OR** capillary random plasma glucose >200 mg/dL

Probable CKDu

- Repeat assessment of eGFR after 12 weeks and eGFR < 60 mL/min using CKD EPI equation **OR** Repeat albuminuria > = 30 mg/g
- Satisfying the exclusion criteria above for 'Suspected CKDu'

  <u>Exclusion criteria to identify probable CKDu among those satisfying above criteria</u>

  i. Diabetes based on fasting plasma glucose >126 mg/dL
  ii. Polycystic kidney, congenital malformation, obstructive nephropathy by ultrasound imaging
  iii. Haematuria of >10 red blood cells/HPF
  iv. Other known causes of CKD such as autoimmune diseases, glomerular diseases, kidney stones or any other obstruction in the urinary tract based on the clinical evaluation **and** laboratory investigations

Confirmed CKDu

- All the above mentioned criteria for probable CKDu
  AND (in addition)
- Histopathological features consistent with CKDu on biopsy, preferably the demonstration of absence of immune deposits

Annex II: Proposed revisions to the formats

1. **Modifications suggested to the formats used in the offline information generation of the sentinel surveillance of CKD** (patients are already confirmed as CKD based on **repeat assessment** of eGFR after 12 weeks and eGFR < 60 mL/min using CKD EPI equation **OR** Repeat ACR > = 30 mg/g)

Already existing variables (Ethnicity and comorbidities can be removed)

S. no	Clinic no	Name	NIC no	Age	Sex	Address	Ethnicity	Occupation	Comorbidities	PHI division	MOH division	GN division

Proposed variables to be added to distinguish Probable CKDu among CKD

A. Serum creatinine (indicate the value) mg/dL	B. eGFR (indicate the value) mL/min	C. Albuminuria (indicate the value) mg/g	D. Urine protein: creatinine ratio > 2 g/g creatinine **or** urine albumin: creatinine ratio > 0.3 g/g creatinine (Yes/**No**)	E. History of diagnosis **or** being on treatment for DM **or** fasting plasma glucose >126 mg/dL in current visit (Yes/**No**)	F. Hypertensives on treatment with more than two drugs **or** Measured BP (preferably using electronic BP apparatus, sitting position, at least two readings one minute apart) SBP>160 **or** DBP>100 (Yes/**No**)	G. Clinical and laboratory evidence of				H. By ultrasound imaging			I. Haematuria >10 red blood cells/HPF (Yes/**No**)	**Probable CKDU** **Yes** *if the responses for ALL the columns from D to I are NO* **No** *if the responses to ANY of the columns from D to I is YES*
						Autoimmune diseases (Yes/**No**)	Glomerular diseases (Yes/**No**)	Kidney stones (Yes/**No**)	Any other obstruction in the urinary tract (also specify) (Yes/**No**)	Polycystic kidney by ultrasound imaging (Yes/**No**)	Congenital malformation (Yes/**No**)	Obstructive nephropathy (Yes/**No**)		

2. Modifications suggested to the formats used in the Community based screening programme in the areas designated as high risk in Sri Lanka

The proposed variables to be included

a. Identification and general information

S no	Name	NIC no	Ethnicity	Current age	Sex	Occupation	Address	mobile number

b. Information to distinguish CKD and Suspected CKDu

A Serum Creatinine (indicate the value) mg/dL	B. eGFR (indicate the value) mL/min	C. Albuminuria (indicate the value) mg/g	D. Urine protein: creatinine ratio > 2 g/g creatinine **or** urine albumin: creatinine ratio >0.3g/g creatinine (Yes/**No)**	E. History of diagnosis of DM **or** being on treatment for DM **or** capillary random plasma glucose >200 mg/dL (Yes/**No)**	F. Hypertensives on treatment with more than two drugs **or** Measured BP (preferably using electronic BP apparatus, sitting position, at least two readings one minute apart) SBP>160 mm/Hg **or** DBP>100 mm/Hg (Yes/**No)**	**CKD** eGFR < 60 mL/min using CKD EPI equation (measurement using standardized methods for creatinine measurement) **or** albuminuria > = 30 mg/g *based on the results of columns B and C* **Suspected CKDu** **Yes** *if the responses for ALL the columns D-F are NO* No *if the responses to ANY of the columns D-F is YES*

3. Modifications suggested to the formats used in the household surveys in the areas designated as high risk in Sri Lanka

Already existing variables

S no	Name	NIC no	Ethnicity	Current Age	Sex	Occupation	Pre existing diagnosis CKD/CKDu Diagnosis Check the medical records and ***indicate the number relevant to what is stated in the records*** i. CKD secondary to known causes ii. CKDu iii. CKD under investigation iv. Suspected CKDu v. Probable CKDu vi. Confirmed CKDu	Age at diagnosis	Address	Phone	Hospital where treated	Date of registration

b. **proposed new variables to be included ONLY for cases of pre-existing diagnosis of CKD where the medical records have not distinguished the Suspect CKDu from CKD**

A Serum Creatinine (indicate the value) mg/dL	B. eGFR (indicate the value) mL/min	C. Albuminuria (indicate the value) mg/g	D. Urine protein: creatinine ratio > 2 g/g creatinine **or** urine albumin: creatinine ratio > 0.3 g/g creatinine (Yes/**No)**	E. History of diagnosis of DM **or** being on treatment for DM **or** capillary random plasma glucose >200 mg/dL (Yes/**No)**	F. Hypertensives on treatment with more than two drugs **or** Measured BP (preferably using electronic BP apparatus, sitting position, at least two readings one minute apart) SBP>160 mm/Hg **or** DBP>100 mm/Hg (Yes/**No)**	**CKD** eGFR < 60 mL/min using CKD EPI equation (measurement using standardized methods for creatinine measurement) **or** albuminuria > = 30 mg/g *Based on the results of columns B and C* **Suspected CKDu** **Yes-** *if the responses for ALL the columns D-F are NO* **No**- *if the responses to ANY of the columns D-F is YES*

Annex III: Draft protocol for community based Chronic Kidney Disease of unknown etiology (CKDu) surveillance

1. Background and justification

Chronic kidney disease of unknown etiology (CKDu) is one of the most important public health problems in Sri Lanka affecting predominantly farmers. Either all or few of the Divisional Secretariat Divisions of 11 districts (out of 25 districts) in the country (Anuradhapura, Pollonaruwa, Kurunegala, Ampara, Trincomalee, Badulla, Mullativu, Vavuniya, Matale, Monaragala and Hambantota) have been designated as 'high risk' for occurrence of CKDu. Though perceived by many to be a disease of high prevalence and with trends of increasing prevalence, none of the current sources of data in the country allows accurate estimation of the burden and trends of CKD or CKDu in the country. Routine morbidity and mortality surveillance through hospital statistics and vital registration systems did not have a specific category for CKD or CKDu. Community based screening programme in areas designated as 'high risk' had challenges of low coverage and lack of exposure related data. The special household survey that has been conducted in the designated 'high risk' areas in 2015, collected information only on the diagnosed CKD/CKDu patients and did not include a method to identify the early asymptomatic cases, precluding the use of the data to estimate prevalence of CKD/CKDu. Data of CKD patients in the Provincial Renal Disease Prevention and Research (PRDPR) Unit was restricted to the North central Province of the country. Though this database was derived from household data and included some exposure data, the period of data collection ranged from 2003 to date with no updating to exclude deaths. Furthermore, none of the sources of data are designed to generate information to formulate hypotheses that could guide further research to identify the causes of CKDu.

World Health Organization (WHO) Country Office for Sri Lanka and Presidential Task Force jointly convened a three-day international expert consultation in April, 2016 which recommended developing a robust surveillance system to understand the burden, geographical distribution and time trends of CKDu in Sri Lanka. It was recommended that the surveillance system should provide a platform for long-term research to understand the role of potential risk factors and document the usefulness of ongoing interventions.

To take forward the key recommendations on surveillance, the National Science Foundation (NSF) and World Health Organization (WHO) Country Office for Sri Lanka jointly organized a two-day workshop on 24th and 25th October, 2016. The workshop provided platform to brainstorm and develop the proposed protocol for community based surveillance. Participants comprised nephrologists, physicians, clinical researchers, non-medical researchers, epidemiologists, program managers at the national/province level and international experts.

2. Objectives

- Estimate the distribution of the eGFR in the selected geographical locations
- Estimate the proportion with eGFR less than 60ml/min and/or albuminuria
- Estimate the proportion with Suspected CKDu
- Compare the proportion with Suspected CKDu within and between the selected geographical locations
- Provide baseline data for possible cohort studies

3. Methods

a. Study design and study sites

Community based cross sectional household survey to be conducted in two districts namely Anuradhapura (highly endemic) and Jaffna (non-endemic) districts.

b. Study population

All the adults above the age of 20 years will be included in the study. Exclusion criteria will be pregnant women and patients undergoing treatment for cancers.

c. Sample size and sampling strategy

The sample size was estimated based on following assumptions: 10% prevalence of CKD, 2.5% absolute precision (20% relative precision), 1.5 design effect (assuming cluster sampling design). The approximate sample size is 830 rounded to 1000 (consistent with the international DEGREE study protocol[1]). The sampling frame will include all the Grama Niladhari Divisions (GND) (primary sampling unit (PSU)) in the district. In each district, total of six (6) GND will be selected. In Anuradhapura district, (consider stratified sampling in the endemic district), data regarding CKD based on screening program is available at GND level. Anuradhapura district will be stratified into three categories based on the screening data i.e. highly endemic, moderately endemic and low level of endemicity. In each category, two GNDs will be randomly selected. GNDs will be randomly selected in Jaffna district. In these districts, majority of the population is rural, therefore at least two third of the selected PSU should be from the rural areas. The aim is to achieve 80% coverage (with a minimum sample size of 1000) to ensure that the burden estimates are correct. Voter lists can be used as a framework for estimating the coverage. Thus, it is expected that approx. 6000 eligible participants will be recruited from each district with the total sample recruited from the two districts being approximately 12000.

[1] Caplin B, Jakobsson K, Glaser J, Nitsch D, Jha V, Singh A, Correa-Rotter R, Pearce N. International collaboration for the epidemiology of eGFR in low and middle income populations: Rationale and core protocol for the Disadvantaged populations eGFR epidemiology study (DEGREE). BMC Nephrology, in press

d. Variables to be included

Both individual and GND level variables will be included in the study. Following major categories of key variables will be included in the survey.

Variables to be collected at the individual level:

i. Socio demographic characteristics
ii. Data to assess whether the case definition of 'Suspected CKDu' is fulfilled.
iii. Behavioral risk factors, history of pre-existing diseases, exposure to environmental risk factors etc. (Table 1)
iv. Anthropometric, blood pressure and lab measurements.

Variables to be collected at the GND level:

These include weather data, water sources in the village, new initiatives to change water source in the recent years, cultivation practices in the village and pesticides/ fertilizer per capita use etc.

Table 1: Key variables to be included for the individual level survey

Domain	Key variables
Geo coordinates	Geographical coordinates of the residence
Socio demographic characteristics	Age, sex, socio economic status, income, housing etc.
Occupation	List the key occupational categories
Family history	CKD, heart disease, diabetes etc.
History of pre-existing diseases	Hypertension, diabetes, CKD, IHD, Kidney stones, cancers, stroke, psychiatric conditions
Intake of drugs	Nephrotoxic drugs, NSAIDs, herbal drugs
Diet	Specific foods: Lotus root, water lily seed powder, lake fish, Star fruit, consumption of salty foods, addition of extra salt
Exposure to pesticides/ fertilizers	Types of use, years/hours of use, use of personal protective measures
Exposure to sun	Years/ hours of use, use of personal protective measures, drinking water habits, tea drinking with sugar
Exposure to animals	Rats/ bats in house, cattle in house, pets in house
Drinking water source	Sources of water for drinking and cooking (history for previous 10 years), history of change of water source, source of water while working in the fields, quantity consumed per day, consumption of treated water
Behavioral risk factors	Smoking, smokeless tobacco, alcohol, second hand smoke etc.
History of infectious diseases	Hepatitis B, C, Leptospirosis
Snake bite	History of snake bite, whether the snake bite was serious enough to require hospitalization

e. Data collection tools

Questionnaire based data collection: The data will be collected using a structured questionnaire. The key elements will include socio demographic characteristics, behavioral risk factors, history of pre-existing diseases, exposure to environmental risk factors etc. (Table 1)

Blood pressure measurements: Blood pressure will be measured using electronic blood pressure measuring apparatus.

Anthropometric measurements:
The height will be measured using a stadiometer and weight will be measured using weighing scale.
Bioimpedence device will be used for the body composition analysis.

Laboratory measurements:
Serum creatinine will be measured by assays calibrated utilizing quality controls traceable to an isotope dilution mass spectrometry (IDMS) standard.

Capillary glucose test will be done and blood samples will be collected for estimating creatinine levels. Urine samples will be collecting for estimating ACR levels

f. Field level implementation plan

A house to house survey will be done to ensure high coverage. The study population will be enumerated using voter's lists. Revisits will be done twice to cover the absentees. Data collection will be done by a dedicated team recruited under the project. Ten (10) individuals per each district who have completed GCE Advanced level will be recruited for data collection. In addition, 2 nurses will also be requited for collection of samples.

The data will be collected using android tablets at the field level. The questionnaire will be developed into an app for use in the android tablets. The online/offline options will be available in the tablet. A sim card will be used in the tablet to transfer the data. A standardized training module will be prepared. The training will have two components, namely classroom and hands on training in the field.

The logistics will be put in place to transport the samples for ACR and serum creatinine. Mechanism for sharing reports with participants with counseling will be established.

Biobanking will be considered after working on the logistics, infrastructure and ethics.

g. Quality assurance

Quality assurance during data collection will be ensured. Intensive supervision will be required in the initial stages. An independent quality assurance mechanism with resurvey in 5% of the respondents can be considered. The equipment should be standardised. An electronic blood pressure measuring apparatus will be used. Quality assurance mechanisms for laboratories should be put in place

h. Human Subjects Protection

Institutional ethics committee approval will be obtained. The written informed consent will be obtained. All the newly diagnosed patients with hypertension, diabetes and chronic kidney disease will be referred to the nearest hospital for treatment.

i. Community surveillance

Repeat surveys will be carried out in the same population every 3 years to document the trends in prevalence and incidence of CKD/CKDu. Resurveys will be done using same protocol and data collection tools. The use of standard identifiers such as NIC number to ensure tracking can be considered. Use of biometry can be considered to track the same individuals.

Annex IV: Design of the cohort study for CKDu

A cohort study will be planned in a subset of the population included in the initial survey. The use of standard identifiers such as NIC number to ensure tracking can be considered. In a selected subsample, cohort will be developed to identify the risk factors and etiology of CKDu. Use of biometry can be considered to track the same individuals. The key objectives and methods as discussed in the group work are summarized below. A detailed protocol will be developed later once the baseline survey is completed.

Objectives

- Estimate the decline in eGFR in a cohort in rural Sri Lanka.
- Determine the risk factors for decline of eGFR

Key components of protocol

- GN areas to be identified from the results of the first round of the survey. The sites with low mean eGFR will be identified based on the survey.
- Participants to the cohort study to be identified among those without suspected CKD at the time of the commencement of the cohort.
- The sample size is estimated to be approximately 300 (to be confirmed later) and the sampling strategy to be decided later.
- Once the participants are recruited for the study, detailed exposures data on individual participants to be collected.
- Exposure data and key lab investigations will be repeated every six months.
- Minimum follow up duration will be 2 years.

Annex V: List of participants

Name	Affiliations
International	
Prof. Neil Pearce	Head of Department of Medical Statistics, Professor of Epidemiology and Biostatistics, London School of Hygiene and Tropical Medicine, UK
Prof. Georgi Abraham	Professor of Medicine, Pondicherry Institute of Medical Sciences, Pondicherry Consultant Nephrologists, Madras Medical Mission, Chennai.
Dr. Prabhdeep Kaur	Epidemiologist, Department of Health Systems, National Institute of Epidemiology, Chennai, India.
Sri Lanka Society of Nephrology	
Dr. Chula Herath	Consultant Nephrologist, Sri Lanka Society of Nephrology
Dr Mathu Selvarajah	Consultant Nephrologist, Sri Lanka Society of Nephrology
Dr Eranga Wijewickrama	Senior Lecturer, Faculty of Medicine, University of Colombo
Ministry of Health, Nutrition and Indigenous Medicine	
Dr. Sarath Amunugama	Director General (Public Health Services 1) Ministry of Health, Nutrition and Indigenous Medicine, Colombo.
Dr Paba Palihawadana	Chief Epidemiologist, Ministry of Health, Nutrition and Indigenous Medicine
Dr. Palitha Bandara	Provincial Director of Health Services. North Central Province
Dr Thilanga Ruwanpathirana	Consultant Epidemiologist, Ministry of Health, Nutrition and Indigenous Medicine
Dr Budhdhi Lokukatagoda	Consultant Community Physician, Ministry of Health, Nutrition and Indigenous Medicine
Dr. Udari Mambulage	Registrar in Community Medicine, Ministry of Health, Nutrition and Indigenous Medicine
Dr Chamly Premajayantha	Medical Officer, Epidemiology unit, Ministry of Health, Nutrition and Indigenous Medicine
Dr. Sameera Senanayake	Senior Registrar in Community Medicine, Family Health Bureau, Ministry of Health, Nutrition and Indigenous Medicine
Dr PCI Rajapakse	Medical Officer Ministry of Health, Nutrition and Indigenous Medicine

Name	Affiliations
Dr N.G.T. Indika	Public Health Inspector, Ministry of Health, Nutrition and Indigenous Medicine
Dr. Roshan Sampath	Consultant Community Physician, North Central province
Dr. U. Bandurathne	Medical Officer, Ministry of Health, Nutrition and Indigenous Medicine, Colombo
Dr. Imesh Prathapasinghe	Medical Officer, Ministry of Health, Nutrition and Indigenous Medicine, Colombo.
Coordinating Secretariat for Science, Technology and Innovation (COSTI)	
Prof. Ajith de Alwis	Project Director, The Coordinating Secretariat for Science, Technology and Innovation (COSTI)
Dr. Sachie Panawala	Project Scientist, The Coordinating Secretariat for Science, Technology and Innovation (COSTI)
Academics /researchers	
Prof. Saroj Jayasinghe	Senior Professor, Faculty of Medicine, University of Colombo
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