Introduction

At the beginning of the 21st century an apparently new form of chronic kidney disease of unknown aetiology (CKDu) had emerged in several areas of Sri Lanka. The CKDu is not related to diabetes, hypertension, snake bite or any other known causes of traditional chronic kidney disease. The disease is characterized by a slow, progressive, asymptomatic development, frequently starting at a younger age group. There is a possible propensity for it to be more prevalent among men engaged in agriculture, typically around the age of 40-60 years.

History of CKDu in Sri Lanka

A range of studies of varying types have been carried out over the last 8 years with a view to elucidating the prevalence, nature & causes of CKDu in several parts of Sri Lanka. According to the data reported in the Annual Health Bulletin 2005, the hospital mortality rate for diseases of the genitourinary system has doubled during the period 1980 to 2005. Several studies have investigated the prevalence of this type of CKDu. However from the studies done so far over a period of 8 years, there has been no concrete evidence to support a particular environmental nephrotoxin. Presence of high levels of fluoride, widespread use of agro-chemicals such as pesticides and heavy metals (e.g. cadmium, lead, uranium) in soil and water sources could be postulated as contributing factors to the high prevalence of CKD in certain areas. As demonstrated in some studies mycotoxins, use of herbal / ayurvedic medicines, smoking and history of snake bite are some other factors to be considered. A combination of two or more of the above factors, possibly a synergistic effect, could also be responsible.
Geographical Distribution of CKDu

The geographical distribution of CKDu appears to be biased towards the North Central Region (NCR) of the country in which North Central, part of North Western and part of Uva provinces are included. The populations at risk are scattered in the North Central Region with high prevalence observed at Medawachchiya, Padaviya, Dehiattakandiya, Girandurukotte, Medirigiriya and recently Nikawewa.

Impact of CKDu

The total number of affected individuals is unknown, but it is thought that in excess of 6000 people are currently undergoing treatment for this condition. In 2005, Anuradhapura Teaching Hospital alone recorded 742 live discharges and 140 deaths due to CKD. Mortality due to genitourinary diseases was the leading cause of death in many districts, being the 11th Leading cause of Mortality in the country. In 2005, about 350 million rupees (4.6% of the Annual Health Budget) was spent on the management of patients with Renal Diseases.
Ministry of Healthcare & Nutrition (MOH)/World Health Organisation (WHO) response to the National effort in addressing CKDu

Request by the Hon Minister of Healthcare and Nutrition

A request was made to WHO headquarters in Geneva, in January 2008 by the Minister of Healthcare & Nutrition Hon. Nimal Siripala De Silva, to assist in elucidating the exact cause for the high prevalence of CKDu in the country. This was done as medical studies done so far have failed to establish a concrete link to any aetiological factor.

In response to this request WHO pledged to send a team to Sri Lanka to carry out a pragmatic & feasible research to elucidate a causative agent.

CKDu Research Seminar

As an initial step towards achieving these objectives, the Epidemiology Unit of the Ministry of Healthcare and Nutrition in association with the World Health Organization organized a seminar on Unusual Occurrence of Chronic Kidney Disease in Sri Lanka, on May 7th & 8th in Colombo. The main objective of this seminar was to review all available information, with a view to providing technical assistance for developing a research proposal to address prevention issues. A panel of International experts was in attendance in addition to all the local researchers and related stakeholders,

Development of the research proposal

A draft research proposal was prepared by the team of experts following this meeting. This research proposal provides a framework for a program of research activities, the main arm of which is to identify the prevalence and main determinant(s) of the chronic kidney disease. This coordinated series of activities is built upon evidence generated by a body of smaller research projects, but was designed to provide a more methodical approach and thereby generate of more conclusive evidence regarding the aetiology of the problem. Once the aetiology is known preventive strategies can be developed and implemented.
Feedback on the research proposal & stake holder meeting

This draft research proposal was shared amongst the relevant stakeholders including the Researchers, Academics, Consultants & Local Authorities for necessary feedback. A three day consultative meeting was held in Polonnaruwa on 3rd, 4th & 5th August.

The complete research effort entails the following different research programmes:

- Case Control study
- Cohort study
- Renal biopsy study (tissue and data collection)
- Environmental study group for case control phase of the study
- Environmental study group for analysis of water for case control study
- Post mortem study group (collection of organs and data)
- Human tissue (post mortem), urine and blood analysis study
- Chronic Kidney Disease registry and Geographical Mapping study
- Study group for analysis of animal tissues study
- Nutrition and Sociology Study

The research proposal is now being finalized prior to commencement of the research effort in October 2008.

The Summary of activities since WHO involvement

<table>
<thead>
<tr>
<th>Month</th>
<th>Year</th>
<th>Activity</th>
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</thead>
<tbody>
<tr>
<td>July</td>
<td>2008</td>
<td>Draft Research Proposal</td>
</tr>
<tr>
<td>August</td>
<td>2008</td>
<td>Circulate and agree content / logistics with academics/clinical/donor communities</td>
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<tr>
<td>September</td>
<td>2008</td>
<td>Peer review and finalize proposal</td>
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<tr>
<td>October</td>
<td>2008</td>
<td>Finalize research groups for main studies &amp; Prepare detailed protocols / questionnaires, and recruit staff – Field Programme Officer/Field workers</td>
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<tr>
<td>November</td>
<td>2008</td>
<td>Priority studies</td>
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<tr>
<td>January</td>
<td>2009</td>
<td>Other studies</td>
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<tr>
<td>July-September</td>
<td>2009</td>
<td>Complete analysis</td>
</tr>
<tr>
<td>December</td>
<td>2009</td>
<td>Complete main report and publications</td>
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<tr>
<td>Beyond</td>
<td>2010</td>
<td>Preventive studies</td>
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There is a need for a comprehensive public health effort to effectively address this problem of CKDu. It is a major public health issue requiring multilevel efforts. This should be taken as a National Priority with joint responsibility resting on Health and Developmental Partners.