Modeling-based Framework for Analysis of Toxin Pathways through Water to Address Some Aspects of Chronic Kidney Diseases with Unknown Etiology (CKDu) in Sri Lanka

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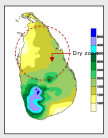
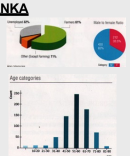
ABSTRACT

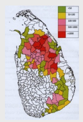
Many hypotheses on contributing factors have been presented on the chronic kidney problem of unknown etiology (CKDu) in Sri Lanka. These include: Arsenic (As) in groundwater from impurities in agrochemicals, Cadmium (Cd) from triple superphosphate, fluoride in the groundwater reacting with other ionic constituents in water such as Ca, Na and Mg, genetic links, effect of Glyphosate in hard water, Cd in food, Cyanobacterial toxins, pesticide and pesticide residues, and overuse, misuse and abuse of agrochemicals, and dehydration, human behavior, among others. The suspected environmental exposure pathways are through water (drinking and cooking water and food) and air (unprotected chemical spraying). Even though extensive data on water quality have been no systematic investigations have been conducted to identify, study and analyze how pathways develop through the water storage and distribution systems and bio-geo-chemical transformations occurring from sources to the receptors where human exposure occurs. This study presents a conceptual model and a system-based framework to conduct such analysis through the use of numerical models of the intergraded surface and subsurface systems with the ability to simulate the fate and transport of naturally occurring toxins, agrichemicals and their geo-bio-chemical transformation products. The modeling tools should be designed to incorporate characterization parameters of the surface water storage and distribution systems, and relevant geo-bio-chemical and hydrogeologic processes in both the shallow and deep aquifers, water quality, and geographical information system (GIS) data, epidemiological data, and climate drivers. Innovations in numerical modeling could be used to downscale climate and regional hydrological model simulation data to evaluate exposure pathways at local scales (e.g., villages) under different climate scenarios and uncertainties.

1 . CKDu in SRI LANKA



Annual rainfall 2540 mm to over 5080 mm in south west of the Island. The North Central Province (NCP) considered "dry zone" rainfall is 1450 mm.





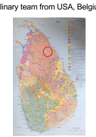
Prevalence of CKDu by Divisional Secretariats (2016-2018)

- ❖ In affected areas 20,828 cases in 2015 compared to 16,479 in 2014.
- ❖ 59,000 patients with estimated 450,000 at risk.
- ❖ Mostly Males (40-60 yrs) working in rice fields.
- ❖ Affected families are often already poor resettled from other areas of the island.
- ❖ Poverty contributes to malnutrition.
- ❖ Reliance on untreated potable water supplies from reservoirs, canals, and wells.
- ❖ Prolonged exposure and latency in diagnosis may be responsible for the disease appearing 15-20 years after causative factors first became present.

2. WORKSHOPS/SITE VISITS (NSF and NIEHS sponsored)

- ❖ August, 2016 - Multidisciplinary team from USA, Belgium, Cuba and El visits Sri Lanka

Spring water non-CKDu village



Location of Padaviya

Meeting with CKDu patients

- ❖ March, 2017- Multidisciplinary team consisting of scientists from USA met with Presidential Task Force, Medical and Geology Faculties at Peradeniya University and HE the President)
- ❖ November, 2017-
  - Special symposium on CKDu at the 17th International Conference of the Pacific Basin Consortium, co-hosted by the Public Health Foundation of India. "Environmental Health and Sustainable Development"
  - Workshop attended by scientists from USA, India and Thailand`
- ❖ June, 2017- A team with expertise in water and environmental systems met with International Water Management Institute (IWMI), Medical and Geology Faculties at Peradeniya University, University of Moratuwa and Sri Lanka National Academy of Sciences). Participated in a IWMI sponsored workshop

3 . CKDu a Global Problem

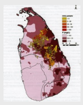
- ❖ CKDu has been recognized as a global health issue in more than a dozen countries in Asia, South America, and the Middle-East.
- ❖ It has been reported that out of these, Sri Lanka is the most affected with the highest cases of CKDu patients and mortality rates.
- ❖ The occupations of the affected population vary from country to country, that includes agriculture and port workers, and cattle farming.
- ❖ Some factors are common but the unknowns in etiology may differ from country to country.

Factor	Sri Lanka	El Salvador
Main population affected	Agricultural population	Agricultural population
Sex of the majority of patients	Male, but also affects women in less degree	Male, but also affects women in less degree
Age range of patients	< 60 y, also affects children??	< 60 y, also affects children, after 11 y of age, boys are more affected than girls.
Poverty and malnourishment	Present	Present
Infectious diseases	Malaria and others	Malaria and others
Education level	Low	Low
Use of nephrotoxic medicaments	NSAIDS, Ayurvedic medicines	NSAIDS
Health services	Dialysis and kidney transplant are available	Dialysis is available in very limited way, and kidney transplant is not available

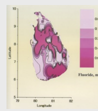
Agrochemicals (pesticides and fertilizers)	Over use, misuse and abuse without protection	Over use, misuse and abuse without protection
Main crop related to the disease	Rice	Sugar cane
Maximum annual ambient temperature	29-33°C (Anuradhapura)	29-37°C (areas affected by CKDu)
Drinking water quality	Water contaminated with F, and probably As, Cd	Water contaminated with As
Ground water aquifers	Mainly secondary porosity aquifers in metamorphic rocks	Mainly secondary porosity aquifers in volcanic rocks
Soils	Reddish Brown Earths and Red Yellow Podzolic soils	Volcanic soils

2. REPORTED FINDINGS ON POTENTIAL FACTORS

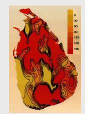
a . Groundwater- Soil, Hardness, Fluoride and CKDu[1]



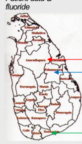
Patient data & fluoride



Fluoride



Hardness



Region	CKD cases	Hardness ($CaCo_3$ mg/l)		Fluoride ($CaCo_3$ mg/l)	
		Maximum	Average	Maximum	Average
Anuradapura	9,005	1373	283	7.0	1.1
Polonaruwa	4,369	980	231	3.4	0.8
Kurunagela	1,706	423	169	5.0	0.7
Matale	1,137	494	120	2.6	0.4
Vavuniya	1,684	665	333	3.1	0.8
Badulla	943	495	140	2.3	0.6
Hambantota	488	1734	293	2.3	0.6
Ampara	468	362	125	5.8	0.8
Moneragala	268	891	244	6.8	1.4
Mullativu	348	619	172	0.4	0.1
Trincolmalee	412	581	254	2.4	0.8
Total	20,258			Sri Lanka Std. 0.6 mg/l	

[1] Kawaksmi et.al, 2014. Groundwater Quality Atlas of Sri Lanka, ISBN 978 955-0597-01-7

- ❖ CKDu affected areas are all located within the dry climatic zone of Sri Lanka where drinking water sources are often limited to shallow water wells which exhibit significant hardness (sum of Ca and Mg usually expressed as $CaCO_3$)
- ❖ Sampled approximately 1300 drinking water wells throughout Sri Lanka and noted that wells in the CKDu endemic region typically exhibited elevated levels of hardness and fluoride; other areas in non-CKDu endemic areas may exhibit elevated hardness or fluoride but generally not both.
- ❖ Combination of hardness and fluoride is contributing to the disease, but these average values do not explain why water from individual wells within the region are not contributing to CKDu.
- ❖ Causes are multifactorial and the variability of water quality from one well to another is controlled by local water and chemical process dynamics.

b . Arsenic and groundwater

Soil map of Sri Lanka (Survey Department of Sri Lanka, 1967)

Region	CKD cases	Arsenic (µg/l)	
		Maximum	Average
Anuradapura	9,005	3	0
Polonaruwa	4,369	3	0
Kurunagela	1,706	1	0
Matale	1,137	2	0
Vavuniya	1,684	2	1
Badulla	943	1	0
Hambantota	488	3	1

Sample data listing CKD cases with arsenic concentrations in wells

- ❖ El Salvador has high levels of arsenic (As); the prevalence of elevated As has not been verified in Sri Lanka.
- ❖ If arsenic is a CKDu cause in Sri Lanka, the question must be asked whether its source is from natural geologic processes or agrochemical use.
- ❖ Survey of 1,304 wells in all districts of Sri Lanka conducted in 2014, found that the As concentration exceeded the drinking water standards of 10 µg/l only within wells located in coastal aquifers.
- ❖ No reported cases of CKDu in these coastal areas where large amounts of fertilizers are used for cultivating papayas and onions.
- ❖ Arsenic concentrations do not have any relationship to the nitrate concentrations in the well water, suggesting that the high levels As is not due to the application of fertilizers but related to the soil conditions.
- ❖ The soil data shows that, in coastal regions, As is "sandy regosol on recent beach and dune sands." In CKDu areas have primarily "reddish brown and law humic grey soil." suggesting that geologic conditions in the CKDu areas also may not be a contributing factor.
- ❖ The observed maximum concentrations are well below the drinking water standards of 10 µg/l. As may not be the cause of CKDu as there are no geologic factors that produce the toxins and measured concentrations are low or non-existent.

c . Cadmium in groundwater[1]

- ❖ One of the adverse effects of Cd is kidney failure.
- ❖ Concentrations of nine heavy metals, including Cd, were measured in the sediments, periphery soils, water, and lotuses (root used as food) of five main reservoirs supplying irrigation water.
- ❖ The concentrations in the reservoir water were found to be significantly higher than WHO standards. The total Cd concentrations in the reservoir sediments in contrast did not exceed the standards of the European Union for agricultural soils.

Region	CKD cases	Cadmium (µg/l)	
		Maximum	Average
Anuradapura	9,005	0.2	0.01
Polonaruwa	4,369	0	0.01
Kurunagela	1,706	0	0
Matale	1,137	0.2	0.01
Vavuniya	1,684	0.1	0.01
Badulla	943	0.1	0.01
Hambantota	488	0.1	0.01

- ❖ Well water quality data study of (Kawakami) et al. (2014)[1] showed that Cd concentrations were below the WHO standard of 3µg/l in in all districts sampled.

d . Agrichemicals

- ❖ Agrichemicals are used in Sri Lanka as fertilizers, herbicides, insecticides, and fungicides.
- ❖ Sime researchers suspected that reservoir water containing Triple Super Phosphate fertilizer (TSP) contaminated with cadmium with concentrations of 0.03 to 0.06 mg/l, when applied in rice fields, caused CKDu.
- ❖ Recent concentrations measurements made by (Chandrajith) et al. (2010) were reported to be in the range 0.0029 - 0.0089 mg/l, much smaller than earlier reported values.
- ❖ Glyphosate based commercially available herbicide, had been widely used in Sri Lanka. It is also heavily used for weed control in tea plantations; however, no reported CKDu.
- ❖ Glyphosate with high solubility (11.6 g/l) can be transported through the surface water as a solute during runoff and adsorbed to colloids. It has considerable adsorption ability, thus resulting in limited mobility.
- ❖ "It could be inferred that the impact on CKDu by the levels of glyphosate and AMPA (Aminomethylphosphonic acid detected in the study area (Nine agricultural fields in Medawachchiya, Anuradhapura District) Sri Lanka, is marginal when compared with the MCL of the USEPA (700 mg/L)"[4]

e . Heat Stress and Dehydration

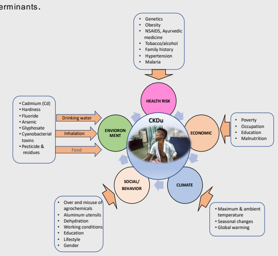
- ❖ The Northern Central Province, which has the highest prevalence of CKDu, is also the hottest region in Sri Lanka.
- ❖ The farmers rigorously and continually work exposed to direct sunlight for long durations under very high temperature throughout the day.
- ❖ Inadequate consumption of water by these farm workers results in chronic dehydration, subsequently making them more susceptible to CKDu.
- ❖ Although dehydration is increasingly being posited as a potential etiologic factor for CKDu in endemic communities, assessment of the associations between dehydration and CKDu across studies was limited by inconsistent reporting of the measurements for assessing dehydration."

f . Genetic variations

- ❖ Genetic susceptibility has been presented and proposed a hypothesis that combines both genetic, environmental and behavioral factors.
- ❖ A study that used whole-exome sequencing to identify the genetic variants associated with CKDu. concluded that, "The past and present genetic analysis also shows that pathogenesis of CKDu cannot be completely explained by genetic factors but, genetic susceptibility enforces a discernible risk for disease occurrence"

3 . MULTIFACTORIAL CHARACTER OF CKDu

Even though the causes of CKDu are not clear, a consensus exists among researchers on its multifactorial character and relation to social, environmental, health risks, and economic determinants.



4 . HYDRGEOLOGY AND WATER DYNAMICS ASSOCIATION

a . Groundwater

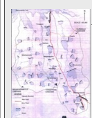
- ❖ CKDu affected region that is classified as a dry zone, 75% of the population relies on groundwater for drinking. Communities relying on spring water, the prevalence of CKDu is very low.
- ❖ As the groundwater users in wet zones are not affected by the disease, it suggests that the recharge replenishes the aquifers, diluting the water and affecting the geochemistry.
- ❖ The geochemistry of the dry zone wells are different in comparison. The annual climatic variations that change the water levels in the aquifers have significant impacts on the quality of the water used for drinking.
- ❖ The groundwater used for irrigation during dry periods and everyday drinking comes from two types of aquifers; the shallow regolith confined to narrow inland valleys in weathered zones does not share a single continuous water table.
- ❖ A total of 15,000 agricultural wells, 5-10 m deep and 5-7 m in diameter, exist within the NCP.
- ❖ The second source of groundwater is located within the deep fractured zones occurring at depths between 30-40m. Potable water comes from both types of aquifers.

[2] Edirisingha et al., 2017. Geochemical and isotopic evidences from groundwater and surface water for understanding of natural contamination in CKDu endemic zones in Sri Lanka, ISOTOPES IN ENVIRONMENTAL AND HEALTH STUDIES, 2017, ISSN: 1025-6016 (Print) 1477-2639

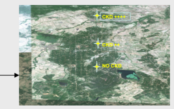
[5] Chandrajith, R., Seneviratne, A, S., Wickramaarachchi, K., Attnanayak,, T., Aturuliya, T. N. C., Dissanayke (2010) Natural radionuclides and trace elements in rice field soils in relation to fertilizer application: study of a chronic kidney disease area in Sri Lanka. Environmental Earth Sciences60, 93-201.

b . Surface water dynamics

- ❖ To understand the water dynamics affecting water availability, it is important to recognize another unique feature of the water distribution system that does not exist in other CKDu affected areas in the world.
- ❖ The NCP is home to a man-made ecosystem based on an ancient irrigation system that goes back approximately 5th century BCE that was modified through a major water diversion project initiated in 1970s.
- ❖ Prior to this project, there had been close to 18,000 manmade ancient reservoirs (referred to as tanks) in Sri Lanka, of which 7,260 are still functional. About 2,000 of the 3,900 reservoirs located in the NCP are still functional. About 2,000 of the 3,900 reservoirs located in the NCP.



Examples of typical cascade system close to Anuradhapura

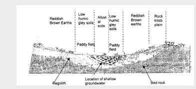


Padaviya tank and canal system

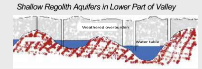
Panabokke, C.R. (2009) Small Village Tank Systems of Sri Lanka: Their Evolution], Setting and Essential Functions, 114 Wijerama Mawatha, Colombo y, Sri Lanka.

c . Hydrogeology

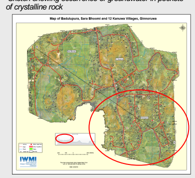
- ❖ "Groundwater regime is confined to a specific topographical location within the cascade and not random across the landscape as commonly envisioned"[1]
- ❖ "Safely exploitable groundwater is mainly confined to those areas immediately adjacent to the main axis of the cascade"[1]
- ❖ Cluster of CKDu shallow wells in Ginnoruwa. These wells are recharged by rainfall only (no surface water)
- ❖ "Medirigiriya area, the groundwater recharged from local rains and local surface water inputs do not associate with CKDu while the groundwater originated from higher elevation rains and travelled through long flow paths up to Medirigiriya is associated with CKDu"[2]
- ❖ "the water table is deeper in the wells associated with CKDu than in non-CKDu wells in Dehiaththakandiya, Padaviya and Medirigiriya during the dry season"[2]
- ❖ "most of the groundwater sources recharged directly from rain and not replenished or mixed with other water sources (stagnant water bodies) have a significant relation with CKDu"[2].
- ❖ "The other groundwater sources that are replenished with surface water inputs have not such a relationship with CKDu"[2]



Shallow Regolith Aquifers in Lower Part of Valley



Sketch showing occurrence of groundwater in pockets of crystalline rock



CKDu wells in two villages in Ginnoruwa

- ❖ "The origin, recharge mechanism and flow pattern of groundwater, as well as geological conditions which would be responsible or natural contaminants in groundwater appear as the main causative factors for the CKDu in the dry zone of Sri Lanka" [2].

5 . RESERCH QUESTIONS

Edirisingha et. al[2] stated the hypothesis that "*the origin, recharge mechanism and flow pattern of groundwater, as well as geological conditions which would be responsible for natural contamination of groundwater appear as the main causative factors for CKDu*"[3]

Focusing on dynamics of water flow and fate and transport of chemicals, the following research questions are raised with the goal of conceptual model:

- ❖ How do the correlations based on regional averages can be used to asses CKDu susceptibility of wells at local scales?
- ❖ What regional and local hydrologic factors contribute to variations in chemical concentrations in wells that are susceptible to producing CKDu conditions?
- ❖ Are the seasonal variations in water levels contribute to significant variation of chemical concentrations in shallow wells to produce CKDu risk?
- ❖ What are the origins of water appearing in wells and the travel times from sources?
- ❖ What are the residence times of potential chemical toxins transported from sources (e.g. agricultural fields & weathering of underground rocks) to the receptor wells?
- ❖ If agrochemicals are a potential cause, what is the fate during its transport from agricultural field to wells, considering the media-dependent half-lives and retardation?
- ❖ How is the climate variability affecting the concentration of chemicals in wells?
- ❖ What processes in the unsaturated zone contribute to variations in chemical concentrations in wells?
- ❖ What are the effects of surface water distribution system based on a cascade of storage tanks and the canal system on the regional and local groundwater quality?

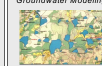
[3] Noble, A., P. Amerasingha, H. Manthrithilake and S. Arsalingam, 2017. Review of Literature on CKDu in Sri Lanka, IWMI Working Paper 158

[4] Gunarathna, S., B. Gunawardana, M. Jayaweera, J. Manatunge, and K., 2018. Zoysa, Glyphosate and AMPA of agricultural soil, surface water, groundwater and sediments in areas prevalent with chronic kidney disease of unknown etiology, Sri Lanka, JOURNAL OF ENVIRONMENTAL SCIENCE AND HEALTH, PART B, 2018, VOL. 0, NO. 0, 1–9

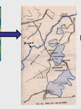
[5] Wickramarathna, S., S. Balassoriya,S. Diyabalanage, and R. Chandrajith, 2017. Tracing environmental aetiological factors of chronic kidney diseases in the dry zone of Sri Lanka—A hydrogeochemical and isotope approach, J. of Trace Elements in Medicine and Biology, 44(2017) 298-306.

6 . CONCEPTUAL MODEL OF WATER FLOW AND TRANSPORT

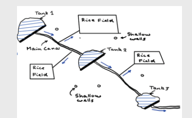
"..conceptual model– a qualitative representation of a groundwater system that conforms to hydrologeological principles and based on geological, geophysical, hydrological, hydrogeochemical principles and other ancillary information" (Anderson et. al., Applied Groundwater Modeling)



System of tanks fed from rain and diverted wet zone water

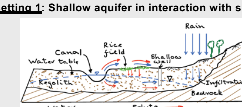


Cascade of tanks



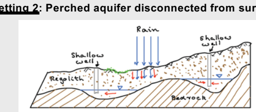
Surface water distribution system associated with the tank cascade

Model setting 1: Shallow aquifer in interaction with surface water



- ➢ The shallow wells withdraw from aquifer that is connected to the surface water distribution system.
- ➢ Chemicals in water is a result of natural processes and from agrochemicals transported through the surface and subsurface water.
- ➢ Natural recharge from rainfall and irrigation water reaches the water table. The fate of the chemicals are controlled by natural reactions in the subsurface.
- ➢ The surface water can dilute the chemical concentrations in the aquifer.

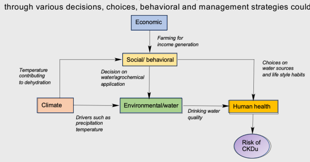
Model setting 2: Perched aquifer disconnected from surface systems



- ➢ The shallow wells withdraw from insolated perched aquifers.
- ➢ The only source of water is natural recharge from rainfall and irrigation water if the wells are in the vicinity of rice fields.
- ➢ The water level fluctuations are seasonal depending on the rain fall.
- ➢ The water level can be very low in the dry season, thus increasing chemical concentrations.

7 . A SYSTEMS BASED APPROCH

- ➢ Systems theory ids defined as "the interdisciplinary study of systems."
- ➢ What is fundamental to the systems approach is that in addition to studying a specific process, phenomenon or mechanism within each system, how the system interacts with other systems are studied to predict the behavior of the whole system.
- ➢ In the case of CKDu epidemic, as the goal is to understand and identify the most significant causal factors to eliminate them or reduce their impact, how the system as a whole behaves in reducing CKDu risk through various decisions, choices, behavioral and management strategies could be determined.



Sub-system interactions of the multifactorial determinants of CKDu.

8 . SUMMARY CONLUSIONS

This paper presented the findings from a number of workshops conducted by a team of scientists who visited Sri Lanka and India to study CKDu in the North Central Province (NCP) in the dry zone of Sri Lanka and some regions in India. A summary of observations and literature reporting on multifactorial factors that contribute to the disease were presented. Based on this information, a set of research questions were developed. A conceptual model that will lead to the development of numerical modeling tools was presented. When developed the model could be used make simulations to address the questions that were raised, better insight into water pathways of chemicals, uncertainty analysis on characterizing parameters, strategies for data collection and predictions of potential effects of climate change.

Acknowledgements

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