



Known to Unknown: Chronic Kidney Disease of Uncertain Aetiology in Sri Lanka, a Deductive Approach

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Abstract

Chronic Kidney Disease is a global health issue as its prevalence is increasing. Sri Lanka is facing a special kind of tubulointerstitial type of nephropathy in certain geographical locations of the island in epidemic proportions of which cause is not certain and it is not related to hypertension diabetes or other conventional known causative factors. Number or environmental toxins are incriminated as a causative factor for this disease. Nearly three decades have passed following identification of the clinical entity, up to date causation had not been established and appropriate public health intervention had not been agreed upon. This opinion paper was developed in order to guide the future researches on this subject after reviewing the literature. Considering the environmental toxins known to cause chronic renal failure and from available data and evidence, it may be concluded that heavy metals lead, cadmium along with fluoride can be considered as more important chemicals. They should be looked in to in researching the CKDu and designing public health interventions to reduce disease burden of CKDu in Sri Lanka. Most scientific and logical approach would be prioritize and investigate the most possible causes and other factors also looked into once the prioritized factors excluded in a resource constrained setting.

Keywords: CKDu; Sri lanka; Chronic kidney disease; CINAC; Lead; Fluoride

Abbreviations: CINAC: Chronic Interstitial Nephropathy among Agricultural Communities; CKDu: Chronic Kidney Disease of Uncertain Aetiology

Introduction

Chronic Kidney Disease is a global health issue as its prevalence is increasing. Sri Lanka is facing an epidemic of special kind of tubulointerstitial type of nephropathy in certain geographical locations of the island of which cause is dubious and it is not related to hypertension diabetes or other conventional known causative factors [1]. It is known as Chronic Kidney Disease of uncertain aetiology (CKDu) or Chronic Interstitial Nephropathy among Agricultural Communities (CINAC). Number of environmental toxins are incriminated as a causative factor for this disease [2]. Nearly three decades have passed following identification of the clinical entity, up to date causation had not been established and appropriate public health intervention had not been agreed upon. This opinion paper was developed in order to guide the future researches on this subject after reviewing the literature.

Discussion

There are number of known environmental toxins that can cause kidney damage. Among them are heavy metals [3,4], pesticides [5], weedicides [5, 6], cyanotoxins [7], fertilizers and hardness of water [8] are some of the broad categories incriminated in causation. In addition, elements like fluoride [9], silica and selenium deficiency [1] are also thought to be associated with the disease causation. Further, number social and environmental factors like poverty, malnutrition, environmental factors on mother, subclinical effects during pregnancy, leading to foetal growth retardation and low birth weight leading to low renal mass which make kidneys more vulnerable to environmental insults are being recognized as associative contributory factors [2].

As comprehensive study of all possible environmental factors associated with chronic human disease in a system dynamic is rather a theoretical approach even though it seems to be the apparently scientific and logical. However, it is a merely impossible task to perform. What is more important to mankind in the public health context is to identify most cost-effective public health intervention or interventions that can reduce the disease burden. Therefore, exclusion of factors from existing knowledge base is the initial rational step for narrowing down the investigation. As we are dealing with a chronic disease with insidious onset it is more likely to be chronic exposure to environmental toxin and factors that are known to cause chronic kidney disease by chronic exposure can be selected. Similarly, factors associated with acute kidney damage can be excluded in resolving the puzzle. By this deduction approach most of the pesticides, weedicides, cyanotoxins, hard water can be put into the lower down in the list of interested factors which have possible causative associations.

Pesticides and weedicides are subjected to intensive premarketing testing for toxicological properties including animal studies prior to release for marketing and they are controlled by regulatory authorities. Some pesticides are known to cause acute kidney injury in acute doses. Agrochemicals with persistent properties in human body or in animals are not permitted to use in open environment. In addition, post marketing surveillance and studying them in exposed people can shed some light into their toxicity. Exposure to agrochemicals occur in people who use them for intended purpose, adventitious exposure and intended self-harm exposure. In Sri Lanka all three forms of exposure pattern are reported and there are no direct convincing evidence to show causal association with the disease in Sri Lanka or elsewhere. This does not mean pesticides are totally safe but they should be placed lower down in the list of probable causative factors of interest for CKDu from the present toxicological knowledge.

Cyanotoxins also known to causes acute liver and kidney injury in animals and humans [7]. There chronic exposure toxicity is not well known. Repeated acute exposure may be a concern but can be in the lower down in the list of probable causative factors of interest. Direct acute toxic effects of fertilizers are known. However low dose chronic exposures are not much described in the literature and they generally believed to be safe and used extensively in agriculture. However, the possibilities of contaminants in the fertilizers. E.g., heavy metals; entering into food chain and causing health impacts is a possibility that has to be taken into consideration [10].

There is no convincing evidence to show use of hard water can cause tubular damage in the kidney. There are ample evidence available people drinking hard water throughout life remain without any significant renal disease. Fluoride is the other important element debated in kidney damage [9]. Higher fluoride concentrations are reported in potable water in disease affected areas. Fluoride is a water-soluble element once entered into the body mainly excreted through kidneys. In high dose exposures which are well beyond natural exposure is reported to be causing

kidney damage in animals [11]. In addition, there are reports of increase absorption of lead and cadmium to the body in the presence of fluoride [12].

In addition, synergistic nephrotoxic effects of fluoride lead, fluoride cadmium are reported [12]. Naturally the kidneys gradually and slowly fail due to ageing. This ageing process may aggravate possibly due to low renal mass and other environmental nephrotoxins. At a certain point of low glomerular filtration fluoride may begin to retain in the body in sufficient concentration to accelerate the kidney damage establishing a downward spiral of adverse outcome leading to worsening of renal failure. Therefore, fluoride may be considered as an important element to consider in chronic renal disease.

Out of the heavy metals, lead cadmium mercury and chromium are known to be associated with kidney damage [7]. Most of early researches on heavy metals are either from occupational exposure or accidental exposures. Considerable concentrations of exposure after becoming adults for some period occurs in occupational settings and whereas acute exposures or something similar to occupational exposure can occur in accidental exposures. With the advancement of environmental toxicology, development of technology to detect heavy metals in nanogram quantities and development of surrogate biomarkers of heavy metal exposure has led to renew the scientific opinion on the human exposures of environmental toxins in ambient environment also. Thereby, reasonable models for chronic low-level exposure models for their health impacts are being developed recently. Out of the heavy metals described above lead may be attributed to low birth weight in addition to nephropathy [13]. Cadmium also incriminated in low birth weight and nephropathy [14]. Therefore, lead and cadmium can be considered more important heavy metals for investigations in order to design a public health intervention.

Conclusion

From the above discussion it may be concluded that heavy metals lead and cadmium along with fluoride can be considered as more important chemicals that should be looked in to in researching the CKDu and designing public health interventions to reduce disease burden of CKDu in Sri Lanka. Priority need to be given for most possible causes and other factors also looked into once the prioritized factors excluded in a resource constrained setting.

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Conflict of Interest

No conflict of interest.

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