

# **Chronic Kidney Disease of Unknown Aetiology (CKDu) and Alleged Presence of Pesticides in Water Sources in Sri Lanka**

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## **Abstract**

Vlahos et al. (2021) have reported the presence of pesticide contamination above safe levels in well water in a region in Sri Lanka where Chronic Kidney Disease of Unknown Etiology (CKDu) is endemic and have drawn a linkage between the two. This claim goes against the generally accepted views on the composition of well water in these regions.

They conclude “*that agrochemical use in ... the Green Revolution ... may now be contributing to ill health, rapid progression of disease, and mortality*”. The authors propose “*reducing ... agrochemical contaminants in Sri Lanka and other tropical countries to reduce ... CKDu*”. These conclusions, tantamount to identifying the aetiology of CKDu, are unsupported by the evidence presented, even at the level of the simplest Bradford-Hill criteria of causation.

Keywords: Chronic Kidney Disease; CKDU, agrochemicals

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## **Introduction**

Chronic Kidney Disease of Uncertain etiology (CKDu) has been extensively studied for over two decades in Sri Lanka, and reported in Central America, India, and certain other locations around the world (Chandrajith et al., 2011; Dharma-wardana et al., 2015; Dharma-wardana, 2018).

In Sri Lanka, the incidence of CKDu has been as high as 15-23% in the North Central Province (NCP) (Wasana et al., 2026; Hettithanthri et al., 2021). These studies have led to the conclusion that those who contract CKDu are essentially those who use water from their own dugout wells; those who use water from springs, rivers, agriculture canals or from wells connected to the water table of the paddy lands do not contract the disease. This has been poignantly shown in comparing the incidence of CKDU in two adjacent villages, known as Badulupura and Sarabhoomi, in the Ginnoruwa area, located in the North Central

Province (NCP) of Sri Lanka. This area receives water from the Mahaweli River (Figure 1).

Studies of well water have implicated the presence of over threshold concentrations of fluoride ions (F<sup>-</sup>) occurring together with Ca<sup>++</sup> and Mg<sup>++</sup> ions (Dharma-wardana 2018, Balasooriya et al. 2020). Many of these studies review or add to the available data on pesticide levels, heavy-metal concentrations, fluoride levels and hardness of the well water used by the residents of the endemic areas.

Furthermore, in the case of those who use water purified via *Reverse Osmosis* (RO) of local water, the waste impurities obtained from RO have been analyzed for pesticide residues and heavy metal traces (Imbulana et al., 2020). All these studies have pointed to very low levels of pesticides or heavy metals, except for the early WHO study that suggested the possibility of higher levels of Cadmium in the water (Jayatilleke et al., 2013).

Several other later studies, including those of Levine et al. (2016), showed that Cd<sup>++</sup> levels in the water and soils of the CKDu endemic regions were way below danger thresholds. However, more recently, Vlahos et al. (2021) have reported the presence of pesticide contamination above safe levels in well water in a region in Sri Lanka where CKDu is endemic. They conclude, based on this single measurement, that:

*“Agrochemical use in paddy and other agricultural practices that have characterized the last 70 years of the Green Revolution in Sri Lanka may now be contributing to ill health, rapid progression of disease, and mortality. Farming, traditionally a highly respected occupation and the well part of the “wealth” of the household, is now a source of danger and a risk”.*

The authors propose “reducing agrochemical contaminants in Sri Lanka and other tropical countries to reduce CKDu”. These conclusions, tantamount to identifying the etiology of CKDu, are unsupported by the evidence presented, even at the level of the simplest Bradford Hill criteria of causation.

In particular, (i) similar non-persistent pesticide excesses have been detected sporadically in most parts of Sri Lanka, including where there is no CKDu; (ii) the pesticides reported in Vlahos et al. (2021) cause both hepatotoxicity and glomerular damage, while CKDu is associated with tubulo-interstitial damage where no hepatotoxic symptoms have been reported; (iii) the pesticides detected are known to be used episodically in farming and have short half-lives; hence the “single time-point” analysis is misleading; (iv) farming communities that use pesticides in the same way but remain essentially without CKDu are found to exist adjacent to those with CKDu; (v) the CKDu prevalence seems to correlate with local geomorphology rather than with farming.

The objective of our study, presented in this article, is to critically review the work of Vlahos et al. (2021) and establish that their results are better explained by a consideration of the geomorphology of the study region.

## Methods

As this study is essentially a critical analysis of material available in published papers, the “materials” and data used here are entirely derived from the existing literature. The data for the geo-morphological analysis are obtained from Google Maps and such sources, as indicated. The “Methods” used involve the application of Bradford Hill criteria (Hill 1965) to determine if the data can be used to go from mere associations to aetiology.

## The Vlahos et al. (2021) Study of CKDu in Sri Lanka

The study area in the Vlahos study is depicted in Figure 1. The area is part of the Accelerated Mahaweli River Irrigation Programme that was implemented in the late 1980s.

A major theme of the Vlahos’ study is the negative effects of the *Green Revolution*. It sharply increased food production, eliminated malnutrition, nearly doubled life expectancy, but also increased environmental pollution. Vlahos et al. (2021) have raised the important issue of the overuse of pesticides in agriculture and their possible role in CKDu.

When CKDu was detected in Sri Lanka, Mesoamerica, India, etc., an agrochemicals etiology was suspected. The favoured suspects were traces of heavy metals, such as arsenic (As) and cadmium (Cd), found in agrochemicals. However, already in 2012, it was evident that heavy metal concentrations in the water and soil in the affected regions were negligible (Nanayakkara et al., 2011), as re-confirmed by subsequent studies (Balasooriya et al., 2020; Jayasiri et al., 2022).

The presence of time-varying amounts of pesticides, such as diazinon (an organophosphorus insecticide) and propanil (a rice herbicide), in aquatic bodies has been reported in many studies. In the recent spatio-temporal study (Jayasiri et al., 2022), pesticides were detected linked to their application times. Given the short persistence lifetimes of about a day or less for diazinon and propanil at 30<sup>o</sup>-36<sup>o</sup> C temperatures, Vlahos et al. (2021) cannot use their “single-time point” data to construct a daily intake and a chronic toxicity assessment.

The time-averaged concentration of these pesticides would be insignificant and not likely to cause chronic toxicity. Furthermore, the well water is largely consumed as brewed tea or in cooking. Such processing removes steam-volatile substances like diazinon. The admissible daily intake (ADI) of, for example, diazinon for chronic toxicity for a 70 kg farmer is 0.14 mg/day, and the aggregate effect of episodic ingestion can be assessed only if urine and blood data are available.

Jayatilleke et al. (2013) detected pesticide residues in the urine of CKDu patients as well as in the controls. The proportions of CKDu subjects with above-reference values for different pesticide residues greater than 5% were: Chlorpyrifos (10.5%), Carbaryl (10.5%), Naphthalene (10.5%). Vlahos et al. (2021) have not reported any urine data or other biopsy data. The pesticides found in the Vlahos study are strongly hepatotoxic (Cakici et al., 2013); their nephrotoxicity manifests as glomerular damage.

In contrast, CKDu shows tubulo-interstitial damage (Nanayakkara et al., 2011) with no signs of hepatotoxicity or other effects typical of these pesticides. CKDu or its rate of progression cannot be correlated with a single-time pesticide measurement in the wells, and the geographic distribution of CKDu

evolution, unless we have time-dependent pesticide data in the blood and urine.



**Figure 1.** Note the Mahaweli River on the left, which drains northwards and the three adjacent farming villages - Badulupura (B), Dolahekaunawa (D) and Saramboomiya (S) in Ginnoruwa. CKDu is not endemic to farmers in S and D (Balasooriya et al., 2020). The wells in the low-lying S, D are connected to agricultural water, but the high-ground wells in B are fed by mineral-rich aquifers. (Adapted from Google Maps).

Shiple et al. (2020) have reported wells highly contaminated with diazinon, etc., in the upper Mahaweli area, where no CKDu exists. Hence, the proposed pesticide aetiology, focusing on diazinon as the most commonly detected pesticide that the authors have linked to CKDu, does not satisfy even simple Bradford Hill criteria for establishing such a linkage [i.e., a statistically valid observed association between a presumed cause (exposure) and an effect (aetiology)]. As discussed below. Hence, in sum, the Valhos et al. (2021) data provide no elucidation of the causes of CKDu or its prevention.

### Bradford-Hill Criteria for establishing aetiology

The Bradford Hill criteria, first proposed in 1965 by Sir Austin Bradford Hill, are **nine** widely used viewpoints in epidemiology and medicine, which provide a framework to determine an association between a presumed cause of a disease (or sickness due to exposure) and an effect (aetiology). Its primary purpose is to assist in ascertaining a true **cause-and-effect relationship** (Hill, 1965). To evaluate whether the pesticide concentrations reported by Vlahos et al. 2021 can be causally linked to the aetiology of CKDu, the data must be scrutinized at least against some of the classic Bradford Hill criteria for causation.

1) **Specificity:** The causal claim fails the test of specificity on two fronts. First, the clinical manifestation of CKDu is strictly characterized by tubulo-interstitial nephritis without significant glomerular or hepatic involvement. In contrast, the primary nephrotoxic profile of the pesticides identified by Vlahos et al. (such as diazinon and propanil) induces acute glomerular damage and profound hepatotoxicity.

Second, the geographic distribution lacks specificity; high levels of these non-persistent pesticides have been documented in areas like the Upper Mahaweli region, where CKDu is virtually non-existent.

2) **Temporality and Biologic Gradient:** A "single time-point" sampling of highly labile, episodic agrochemicals cannot establish a chronic exposure timeline or a biological dose-response curve. Given the rapid environmental degradation half-lives of these compounds at tropical temperatures (30–36 °C), a single spike does not equate to the decades of sustained exposure required to induce chronic renal failure.

**Consistency:** The proposed agrochemical aetiology lacks consistency. Farming communities across Sri Lanka utilize identical Green Revolution agricultural inputs and pesticide regimens, yet the high prevalence of CKDu remains tightly confined to specific endemic

hydrogeological pockets within the North Central Province (NCP). Consequently, the association presented by Vlahos et al. (2021) reflects a transient environmental occurrence rather than a plausible causal mechanism for CKDu.

### Implications for CKDu from the Geomorphology of the Ginnoruwa region

Vlahos et al. (2021) have largely ignored the fact that the wells they have studied are situated in terrain similar to that of Badulupura (which is close to Wilgamuwa, the region of the Vlahos study). The CKDu-affected residents of the Ginnoruwa region live on high ground where the geomorphology differs from that of the areas where there is no CKDu. It is this geo-morphological difference that ensures that there are higher levels of fluoride ions and hardness in the wells located in high ground, unlike the wells located in the lower elevations. The use of water from the latter is not associated with a CKDu risk.

CKDu prevalence may be correlated with the presence of fluoride and Mg, Ca ions in detailed studies. However, even an examination of the local geomorphology, as seen from the map of Ginnoruwa, 15-20 km South-East of Wilgamuwa, studied in Vlahos et al. (2021), is sufficient to bring out a difference between the two areas, of which only one is endemic to CKDu.

As shown in **Figure 1**, Ginnoruwa has three farming villages: Badulupura (B), Dolahekanuwa (D), and Sarabhoomiya (S). All three were settled in the 1980s. However, while most families in B have at least one CKDu patient, those in D and S have virtually no CKDu patients (Balasooriya et al., 2020).

**Figure 1** also shows that Badulupura is in rocky high ground where the drinking-water wells are fed from regolith aquifers, while the wells in the CKDu-free low-lying D and S regions are connected with the water table of the paddy fields, as established using isotopic tracer studies (Edirisinghe et al., 2017). The well water in Badulupura (B) contains excessive concentrations of fluoride and magnesium ions (Balasooriya et al., 2020).

Similar excessive fluoride and magnesium concentrations have been found in reverse-osmosis filtration residues in other endemic regions (Imbulana et al., 2020), while no significant agrochemical residues were detected. Combinations of Mg<sup>++</sup> and F<sup>-</sup> ions are suspected to synergistically cause CKDu (Dharma-wardana, 2018). So, it is natural to ask if the CKDu-associated wells of the Vlahos study have excess concentrations of Mg<sup>++</sup> and F<sup>-</sup>.

## Results and Discussion

Our critical review indicates that the localized prevalence of CKDu cannot be explained by uniform agricultural pesticide application. On the other hand, there is strong evidence from multiple studies, conducted over many years by different research groups, that correlates the prevalence of CKDu with regional geomorphology and groundwater hydro-geochemistry.

Agrochemical inputs are distributed broadly across both endemic and non-endemic farming zones. However, the incidence of CKDu selectively tracks households relying exclusively on private, shallow dugout wells tapping a specific regolith aquifer matrix.

This geo-morphological dependency is sharply illustrated by the epidemiological divergence between the adjacent villages of Badulupura and Sarabhoomiya in Kebithigollawa. While both communities share identical socio-economic profiles, dietary habits, and agricultural pesticide practices, CKDu is highly endemic in Badulupura but nearly absent in Sarabhoomiya.

Geo-morphological mapping reveals that Sarabhoomiya is situated near natural springs and rapid-flushing drainage paths, whereas Badulupura sits on a low-gradient, high-evaporation terrain underlain by metamorphic bedrock. This setup promotes long groundwater residence times and deep mineral leaching.

The unique crystalline bedrock of the endemic NCP zones accelerates the subsurface weathering of minerals, enriching the dugout well water with elevated concentrations of fluoride (F<sup>-</sup>) ions alongside calcium (Ca<sup>2+</sup>) and magnesium (Mg<sup>2+</sup>) hardness. When ingested, these ions form stable chemical complexes that selectively damage the renal tubules over time. This dynamic directly aligns with the observed tubulo-interstitial pathology of CKDu.

Furthermore, the domestic processing of well water—primarily boiling it for brewed tea or cooking—volatilizes steam-volatile pesticide residues, such as diazinon, drastically reducing human ingestion well below the Admissible Daily Intake (ADI) thresholds.

The lack of corresponding pesticide biomarker data (in blood or urine) in the Vlahos et al. study further weakens the claim that these short-lived agrochemicals reach systemic, nephrotoxic concentrations in the local population. Thus, the spatial clustering of CKDu is fundamentally driven by the interaction between local geomorphology and drinking water hydro-geochemistry, rather than modern agrochemical runoff.

## Conclusions

In conclusion, the Vlahos et al. (2021) study, a single-time measurement of pesticide concentrations, is totally inadequate to state anything useful regarding the incidence of CKDu in the North Central Province of Sri Lanka. Furthermore, Vlahos et al. (2021) have not measured in their study or taken into account the fluoride concentrations and hardness of the well water. Both factors are now accepted as being very likely to be linked to the incidence of CKDu in Sri Lanka. As discussed above, therefore, to draw a causal link between “Green Revolution” and its agricultural successes, presumably through the use of agrochemicals (fertilizers, herbicides and crop protection chemicals) and CKDu is unwarranted.

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