# Heavy metal exposure and CKDu; Sri Lankan Perspective

# Chronic kidney disease of uncertain aetiology: prevalence and causative factors in a developing country

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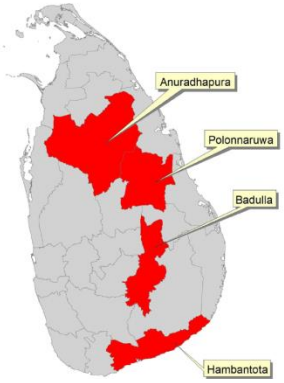


**Table 3 Urine concentration of arsenic, cadmium and lead for CKDu cases compared with controls from the endemic and non-endemic areas**

| | Mean, median (range) of concentration in urine (µg/g creatinine) | | |
|---|---|---|---|
| | Arsenic | Cadmium | Lead |
| CKDu cases ($n = 495$) | 45.447, 26.3 (0.4 to 616.6) | 1.039, 0.695 (0.005 to 8.93) | 1.153, 0.95 (0.04 to 8.53) |
| Controls from endemic area ($n = 132$) | 92.443, 6.99 (0.2 to 966.29) | 0.646, 0.18, (0.005 to 5.13)[a] | 1.254, 0.793 (1.21 to 6.64) |
| Controls from non-endemic area ($n = 250$) | 56.572, 42.025 (5.38 to 350.28) | 0.345, 0.265 (0.005 to 2.079)[b] | 2.099, 1.434 (0.277 to 20.9) |

[a] Urine cadmium concentration of cases compared to controls from endemic area $P < 0.001$.
[b] Urine cadmium concentration of cases compared to controls from non-endemic area $P < 0.05$.

- **Urine Cadmium was significantly higher than controls both from endemic and non-endemic areas.**
- **There was no significant difference in urinary Arsenic and Lead levels in CKDu cases in comparison to controls**
- **Cadmium in nails was significantly higher in CKDu cases (mean 0.017 vs 0.009), ($p<0.05$).**
- **No significant difference in cadmium in hair**

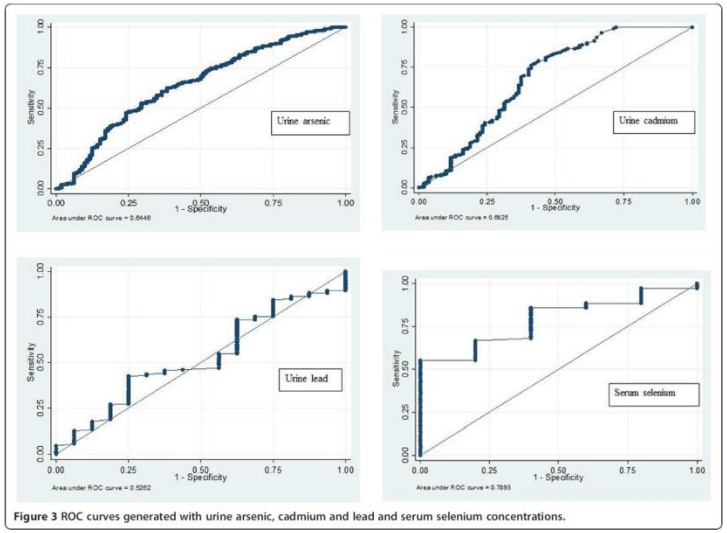


Figure 3 ROC curves generated with urine arsenic, cadmium and lead and serum selenium concentrations.

Dose–response analysis showed that cadmium exposure is a risk factor for the development of CKDu: P = 0.019 for stage 3 and P = 0.024 for stage 4.

There was no significant dose–effect relationship between the urinary arsenic or lead and the stage of CKDu.

The sensitivity and specificity for U Cd concentrations were 80% and 53.6% respectively (AUC = 0.682, 95% CI = 0.61 to 0.75, cut-off value ≥0.23 µg/g).

The sensitivity and specificity for the concentration of arsenic in urine were 90% and 23.2% respectively (AUC = 0.64, 95% CI = 0.58 to 0.71, cut-off value ≥88.57 µg/g).

The concentration of lead in urine was a poor predictor of CKDu (AUC = 0.53, 95% CI 0.38 to 0.67).

# Urinary Cd excretion µg/g Cr

| CKDu patients<br>Mean Median (Range) | Controls in endemic areas<br>Mean Median (Range) | Controls in non endemic areas<br>Mean Median (Range) | Non farmer controls in non.endemic<br>Mean Median (Range) | |
|---|---|---|---|---|
| (n=495)<br>1.039, 0.695 (0.005 to 8.93) | N=132<br>0.646, 0.18, (0.005 to 5.13)[a] | N=250<br>0.345, 0.265 (0.005 to 2.079)[b] | | Jayathilake et al (2013) |
| (n= 18)<br>0.788 (0.549) | (n=18)<br>0.571 (0.289) | (n=8)<br>0.390 (0.172) | | Chandrajith et al (2010) |
| (n=35)<br>0.68<br>0.57<br>(21.25-58.09) | | (n=37)<br>1.30 p<0.001<br>0.91<br>(0.73-1.69) | (n=35 )<br>0.56<br>0.48<br>(0.32-0.68) | Wanigasuriya et al (2018) |

U Cd associated with onset of renal injury 2µg/g Creatinine

U As levels were higher than US population data

# Cadmium National Research Team Study. *Jayathilake et al*

| | endemic area | non-endemic area | Accepted level |
|---|---|---|---|
| Surface soil | Mean 1.16 µg/g (n = 94) | Mean 0.49 µg/g (n = 45) | |
| Lotus root | Mean = 0.413<br>median = 0.066 mg/kg<br>maximum = 1.50 mg/kg | mean = 0.023<br>median = 0.023 mg/kg<br>maximum = 0.44mg/kg | |
| Tobacco | Mean = 0.351 mg/kg<br>median = 0.351 mg/kg<br>maximum = 0.44 mg/kg | Mean = 0.316 mg/kg<br>median = 0.316 mg/kg<br>maximum = 0.351 mg/kg | |
| Vegetables | Maximum = 0.322 mg/kg | Maximum=0.063 mg/kg | The maximum levels Codex Alimentarius for vegetables is 0.2 mg/kg |
| Fish | Maximum level = 0.06 µg/g | | European maximum limit of 0.05 mg/kg |
| Rice | 0.033 mg/kg | 0.018 mg/kg | Codex Alimentarius allowable limit (0.2 mg/Kg) |

? Weekly tolerable uptake

# Heavy metals in Drinking water

| | Type of water | Arsenic µg/L | Cadmium µg/L | Lead µg/L |
|---|---|---|---|---|
| Chandrajith, 2011 | Drinking water | < 0.015 – 0.922 | <0.003 – 0.033 | < 0.046 – 0.957 |
| | Reservoirs | | 0.0029-0.0081 | |
| | Water in NCP | <10 | | |
| Jayawardene et al 2012 | Well water NCP | 0.03 - 3.6 | 0.00 – 0.03 | 0.0 – 0.4 |
| Jayathilake et al 2012 | Water in NCP* | < 10 | < 3 | < 10 |

Allowed limits (WHO) As= 10 µg/L, Cd=3µg/L, Pb =10 µg/L

**Quest to identify geochemical risk factors associated with chronic kidney disease of unknown etiology (CKDu) in an endemic region of Sri Lanka—a multimedia laboratory analysis of biological, food, and environmental samples**

Keith E. Levine · Jennifer Hoponick Redmon · Myles F. Elledge · Kamani P. Wanigasuriya · Kristin Smith · Breda Munoz · Vajira A. Waduge ·

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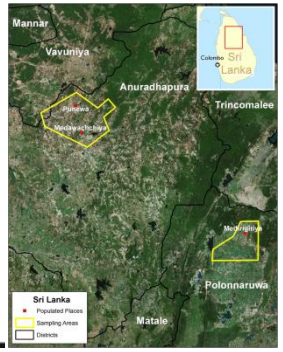


Whole blood Cd and blood concentrations exceeded mean US reference values from healthy nonsmokers for 68.7 and 89.2 % of the samples, respectively (CDC 2015). (n=85)

Cd in hair did not exceeded US mean reference values for women

Rice—The maximum measured Cd rice concentration was below the Codex Alimentarius Commission reference level and MAC for Chinese rice.

Fish—Observed concentrations were similar to or lower than other recent literature reports (Jayatilake et al. 2013; Bandara et al. 2007).

Soil- As, Cr, Cu, Fe, Hg, Mn, Ni, Pb, and Se concentrations exceeded mean background US soil concentrations. No study samples exceeded maximum background US soil concentrations.

## Limitations

1. All the studies are cross-sectional  (snap-shot).
2. Exposure levels (Weekly tolerable doses) are not measured.
3. Data on biological samples are not consistent and shows no definite evidence of high levels
4. Water permissible levels in all the studies