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Decreasing incidence of hospital diagnosed CKD/CKDu in North Central Province of Sri Lanka: is it related to provision of drinking water reverse osmosis plants?

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Abstract

Background We assessed the possible impact of provision of reverse osmosis (RO) water on the incidence of hospital diagnosed CKD/CKDu in North Central Province (NCP) of Sri Lanka.

Methods An ecological study was conducted on data from 2010–2020 on the incidence of hospital diagnosed CKD/CKDu, CKD/CKDu screening and provision of drinking water RO plants in NCP. Analysis was conducted using descriptive statistics, ANOVA and chi-square test.

Results The annual incidence of hospital diagnosed CKD/CKDu (per 100 000 population) in 2010–2013, 2014–2016 and 2017–2020 periods in Anuradhapura district were 129.07, 331.06 and 185.57 ($p=0.002$) while in Polonnaruwa district these were 149.29, 326.12 and 296.73 ($p=0.04$) respectively. In NCP provision of RO plants commenced after 2011 and the decline in the incidence of hospital diagnosed CKD/CKDu was seen in 25 of the 29 Divisional Secretary Divisions when more than 20% of the families received access to drinking RO water projects.

Conclusions The annual incidence of hospital diagnosed CKD/CKDu increased in NCP from 2010 to 2016 and continuously decreased thereafter. Continuous declining of CKD/CKDu incidence was seen after more than 20% of the families received access to drinking water RO plants.

Key message

The incidence of hospital diagnosed CKD/CKDu in CKDu affected North Central Province of Sri Lanka is decreasing possibly due to provision of safe drinking water.

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Keywords (CKDu) Chronic Kidney Disease of uncertain origin, Decreasing incidence of CKD/CKDu, Provision of safe drinking water

Introduction

Chronic kidney disease of uncertain origin (CKDu) was first identified in Sri Lanka in early 1990s from Madawachchiya Divisional Secretariat (DS) Division in the Anuradhapura district [1]. Two decades later it was endemic in the North Central Province (NCP) and had spread to bordering districts as well [2]. Despite many studies the cause of CKDu still remains elusive [3–10]. Nevertheless, most of these CKDu causation hypotheses linked drinking water as the source of entry of the injurious agent to the human body [11]. The water in NCP is hard and unpalatable [12, 13] resulting in residents drinking inadequately to quench their thirst [14]. Based on this hypothesis the government commenced provision of reverse osmosis (RO) water [15, 16]. This was supplemented by health education programmes to promote adequate drinking of safe water [17]. A recent publication described a decrease in the incidence of CKDu in NCP possibly due to provision of safe drinking water [2]. In this study we analyzed the possible impact of provision of RO water on the incidence of hospital diagnosed CKD/CKDu in North Central Province of Sri Lanka.

Methods

This was an ecological study looking at population level data on the incidence of hospital diagnosed chronic kidney disease (CKD)/CKDu, CKD/CKDu screening and provision of RO water in North Central Province. The methodology for assessing the incidence of hospital diagnosed CKD/CKDu in NCP was previously described in detail [2]. To calculate the incidence of hospital diagnosed CKD/CKDu, all newly diagnosed patients were prospectively collected from 11 hospitals on a monthly basis. The hospitals included Teaching Hospitals, District General Hospitals, Base Hospitals and Divisional Hospitals of the Anuradhapura and Polonnaruwa districts. The diagnosis of CKD (which includes CKD and CKDu) and staging of the disease had been made by a Nephrologist or Consultant Physician according to the Kidney Disease: Improving Global Outcomes paper [18]. The GFR estimations were derived using the CKD-EPI creatinine Eq. [19]. As the definitive guidelines for distinguishing CKD from CKDu (in Sri Lanka) according to World Health Organization criteria became available only after 2016 [20], attempts were not made to distinguish between CKD and CKDu. Although an early guideline for case

definition of CKDu was available [3] we observed during GIS mapping of CKD/CKDu patients [2] that the Nephrologists/Consultant Physicians in Anuradhapura and Polonnaruwa did not use this guideline and documented most CKDu cases as CKD.

The CKD/CKDu screening information from 2010–2020 was obtained from the Regional Director of Health Services of Anuradhapura and Polonnaruwa districts. The formal organized screening programmes in NCP were initiated in 2014. Screening was conducted using urine albumin to creatinine ratio and serum creatinine. Estimation of urine albumin to creatinine ratio and serum creatinine was done at the nearest hospital laboratory. Urine albumin to creatinine ratio of greater than 30 mg/g or eGFR less than 60 ml/1.73m²/min were considered as screening positive and referred to nearest government hospital [21]. CKD/CKDu high incidence DS divisions were given priority, thus high proportions were screened in these areas. In the North Central Province concerning CKD/CKDu, there exist villages with both high and low incidence rates. However, irrespective of the hospital-diagnosed incidence rates at the village level, all individuals were given an equal opportunity to undergo CKD/CKDu screening when it was conducted. There was no prioritization based on age, sex, or any other factor during the screening process.

The information with regard to RO plants were gathered routinely by the National Renal Disease Prevention and Research Unit (NRDPRU) of the Ministry of Health, Sri Lanka. NRDPRU conducts surveys in DS Divisions of NCP to map the drinking water RO plants as provision and management of drinking water RO plants is part of their responsibility. To date more than 1,000 drinking water RO plants have been provided to NCP. Before visiting the DS Division for the drinking water RO plant survey, a map of the CKD/CDKu patients in the area along with main roads was created using ArcGIS. ArcGIS is a Geographic Information System (GIS), which is used to display geographic data and create maps. Information on drinking water RO plant locations were gathered on each Gramaniladhari (GN) division of DS Divisions separately from the existing database of NRDPRU. A GN Division is the smallest administrative division in the country and each DS Division in NCP is made up of more than 25 GN Divisions. During the survey, drinking water RO plants provided and managed through other organizations were

searched by interviewing key informant field officers (eg. Gramasewaka, Samurdhi Officer, and Agriculture Officers) and private drinking water suppliers of the GN Division. The operator of the RO plant was also interviewed separately to obtain the required information.

The data gathered was statistically analyzed using STATA 13 student version. Counts and percentages were used to express discrete variables while mean and standard deviation were used to express continuous variables. For analysis purposes we divided the study population into two time segments as follows: the period of increasing incidence of hospital diagnosed CKD/CKDu from 2010 to 2016 and the period of decreasing incidence from 2017 to 2020. The first segment was further divided into two time segments: where CKD/CKDu formal organized screening was not conducted (from 2010 to 2013) and CKD/CKDu formal organized screening had commenced (from 2014 to 2016). To calculate the incidence, population data was obtained from the 2011 Census [22] and expressed as per 100,000 population. All incidence rates calculated were annual rates. The annual hospital diagnosed CKD/CKDu incidence increase rate was calculated by subtracting the incidence of the current year from the previous year.

Results

During 2010 to 2020 period 362,293 and 205,767 were screened for CKD/CKDu, in Anuradhapura and Polonnaruwa districts respectively. In Anuradhapura district the highest number of population was screened in 2016 (89, 184) and in Polonnaruwa in 2017 (44, 681). Average proportion of population annually screened for CKD/CKDu in both districts was 6.7% (3.1 SD) and 8.5% (2.2 SD) respectively. From 2015 to 2020, In Anuradhapura district, among DS divisions, those with the six highest incidence of hospital diagnosed CKD/CKDu (annual hospital diagnosed CKD/CKDu incidence of > 500 per 100,000 population from 2014 to 2016) three had screened more than 50% of the population while among the six lowest DS divisions (annual incidence of < 185 per 100,000 population from 2014 to 2016) 4 had screened less than 23% of the population. In both districts a higher proportion was screened from 2014 to 2016 period.

There were a total of 30,596 new hospital diagnosed CKD/CKDu patients reported from NCP during the period of 2010 to 2020 (19,378 and 11,218 from Anuradhapura and Polonnaruwa districts respectively). The incidence of hospital diagnosed CKD/CKDu increased from 2013 to 2016 and continuously declined thereafter in both districts. Table 1 compares the selected characteristics of the annual incidence of hospital diagnosed CKD/CKDu, CKD/CKDu screening details and provision of drinking water RO plants in Anuradhapura and

Polonnaruwa districts from 2010–2013, 2014–2016 and 2017–2020 period.

The annual rate of increase of hospital diagnosed CKD/CKDu incidence was highest for Anuradhapura district (158.7) in 2014 while for Polonnaruwa district (143.6) this was observed in 2016. The annual rate of decrease of hospital diagnosed CKD/CKDu incidence was highest for Anuradhapura district in 2017 (105.4) while for Polonnaruwa district this was observed in 2020 (136.4).

Figure 1 shows the incidence of hospital diagnosed CKD/CKDu, CKD/CKDu screening proportion and the percentage of families receiving RO plant water from 2010 to 2020 in Anuradhapura and Polonnaruwa districts and Fig. 2 demonstrates these at each DS divisions of NCP.

Figure 3 illustrates the distribution of incidence of hospital diagnosed CKD/CKDu in NCP for the years a) 2010, b) 2016 & c) 2019 and the availability of RO water in d) 2016 and e) 2018.

Discussion

The occurrence of CKD/CKDu has previously shown a clustering pattern (Fig. 3) with highly endemic areas being clustered closely together [2]. Areas with a high incidence of hospital diagnosed CKD/CKDu are located mainly within the NCP together with DS divisions of adjacent districts [2, 23]. The incidence of hospital diagnosed CKD/CKDu decreases gradually from the epicenter of high incidence areas [2]. This may be because environmental factor/factors contributing to CKDu reduce gradually when moving away from the epicenter of high CKD/CKDu incidence areas.

The incidence of hospital diagnosed CKD/CKDu in Anuradhapura and Polonnaruwa districts increases from 2010 to 2016 and thereafter decreases (Fig. 1). The incidence of hospital diagnosed CKD/CKDu in all DS divisions of Anuradhapura and Polonnaruwa districts demonstrate a more or less similar trend (Fig. 2).

During the early period of our study a high proportion of the diagnosed CKD would have been CKDu. With the prevalence of diabetes increased to 16.5% in NCP [24] and the prevalence of hypertension increased to 26% in Anuradhapura district [25] towards the later part of our study, a significant portion of CKD in NCP may be related to hypertension and diabetes, in comparison to 2009 when the first paper on CKDu was published [26]. Hence, the possibility of a significant dilution of the study sample by diabetes/hypertension-associated CKD must be acknowledged. In this view the actual CKD figures towards latter part of the study should increase considering the increased prevalence rates of diabetes and hypertension. Therefore, this may also indicate the declining incidence is actually involves the CKDu proportion. As

Table 1 Selected characteristics of the incidence of hospital diagnosed chronic kidney disease / chronic kidney disease of uncertain origin, screening details for chronic kidney disease / chronic kidney disease of uncertain origin and provision of drinking water reverse osmosis plants in Anuradhapura and Polonnaruwa districts from 2010–2016 period and 2017–2020 period

Characteristics	Anuradhapura (total CKD/CKDu patients = 19 378)			Level of Significance	Polonnaruwa (total CKD/CKDu patients = 11 218)			Level of Significance
	2010 to 2013	2014 to 2016	2017 to 2020		2010 to 2013	2014 to 2016	2017 to 2020	
Total CKD/CKDu cases	4443 (22.9%)	8547 (44.1%)	6388 (33.0%)		2425 (21.6%)	3973 (35.4%)	4820 (43.0%)	
Mean annual incidence of hospital diagnosed CKD/CKDu (per 100 000 population)								
District (SD)	129.07 (8.46)	331.06 (50.10)	185.57 (71.09)	$F = 14.17$ $P = 0.0024$	149.29 (34.81)	326.12 (98.80)	296.73 (104.11)	$F = 4.79$ $P = 0.042$
Male population (SD)	175.73 (9.95)	406.73 (60.23)	253.93 (93.29)	$F = 11.00$ $P = 0.0051$	215.41 (44.88)	424.51 (115.41)	374.79 (137.03)	$F = 3.93$ $P = 0.0649$
Female population (SD)	84.57 (9.90)	258.89 (40.55)	120.38 (50.23)	$F = 20.07$ $P = 0.0008$	84.63 (25.30)	229.90 (84.31)	220.40 (72.76)	$F = 6.24$ $P = 0.0233$
< 39 years age group (SD)	14.59 (1.94)	41.05 (6.22)	23.36 (5.24)	$F = 28.46$ $P = 0.0002$	17.31 (11.61)	52.67 (20.88)	40.35 (17.81)	$F = 4.13$ $P = 0.0585$
40–59 years age group (SD)	289.47 (6.71)	708.27 (106.11)	360.11 (156.57)	$F = 13.76$ $P = 0.0026$	281.50 (74.58)	582.92 (178.88)	516.16 (186.96)	$F = 3.97$ $P = 0.0635$
> 60 years age group (SD)	575.68 (67.45)	1559.25 (292.80)	962.95 (350.71)	$F = 11.99$ $P = 0.0039$	695.47 (110.92)	1500.70 (425.02)	1451.66 (489.57)	$F = 5.52$ $P = 0.0002$
Annual average incidence increase rate (SD)	-3.64 (18.38)	86.30 (62.78)	-69.66 (40.56)	$F = 10.82$ $P = 0.0072$	26.10 (39.30)	79.13 (55.81)	-70.67 (44.20)	$F = 9.38$ $P = 0.0104$
No. of DS which showed a declining hospital diagnosed CKD/CKDu incidence (Anuradhapura $n = 22$; Polonnaruwa $n = 7$)	1	6	15		0	0	7	
CKD/CKDu Screening details								
Total screened (annual mean) [SD]	-	154 032 (77,016) [21,237.25]	208 261 (52,065.25) [29,998.66]	$F = 1.05$ $P = 0.3627$	-	75 826 (37,913) [1742.31]	129 941 (32,485.25) [10,692.61]	$F = 0.45$ $P = 0.5373$
Screened % from population (annual mean) [SD]	-	14.34% (7.17) [1.09]	22.36% (5.59) [3.60]	$F = 0.33$ $P = 0.5954$	-	16.31% (8.15) [7.41]	29.64% (7.41) [3.59]	$F = 0.08$ $P = 0.7962$
No. of DS divisions with highest annual number screened (Anuradhapura $n = 22$; Polonnaruwa $n = 7$)	0	14	8		0	5	2	

Table 1 (continued)

Characteristics	Anuradhapura (total CKD/CKDu patients = 19 378)			Level of Significance	Polonnaruwa (total CKD/CKDu patients = 11 218)			Level of Significance
	2010 to 2013	2014 to 2016	2017 to 2020		2010 to 2013	2014 to 2016	2017 to 2020	
No. DS divisions with highest annual number screened occurring on or after decline of hospital diagnosed CKD/CKDu incidence (Anuradhapura <i>n</i> = 22; Polonnaruwa <i>n</i> = 7)	0	2	7		0	0	2	
No. of DS divisions with highest annual number screened occurring before decline of hospital diagnosed CKD/CKDu incidence (Anuradhapura <i>n</i> = 22; Polonnaruwa <i>n</i> = 7)	0	12	1		0	5	0	
Details of RO plants								
No. of new RO plants	25	353	378		4	124	111	
No. of new beneficiary families (%)	4743 (2.0%)	74,951 (31.2%)	84,289 (35.1%)	<i>F</i> = 2.62 <i>P</i> = 0.1329	1060 (1.0%)	25,919 (27.1%)	51,673 (47.6%)	<i>F</i> = 4.96 <i>P</i> = 0.0397
Provision of drinking water RO plants to DS Divisions (Anuradhapura <i>n</i> = 22; Polonnaruwa <i>n</i> = 7)								
No. of DS which commenced RO projects (%)	9	13	0		2	5	0	
No. of DS with < 20% families getting RO water	22	7	0		7	3	0	
No. of DS with > 20% families getting RO water (%)	0	15	7		0	4	3	
No. of DS with > 20% families getting RO water on or before decline of hospital diagnosed CKD/CKDu incidence	0	6	12		0	0	7	

Table 1 (continued)

Characteristics	Anuradhapura (total CKD/CKDu patients = 19 378)			Level of Significance	Polonnaruwa (total CKD/CKDu patients = 11 218)			Level of Significance
	2010 to 2013	2014 to 2016	2017 to 2020		2010 to 2013	2014 to 2016	2017 to 2020	
No. of DS with > 20% families getting RO water after decline of hospital diagnosed CKD/CKDu incidence	1	1	2		0	0	0	

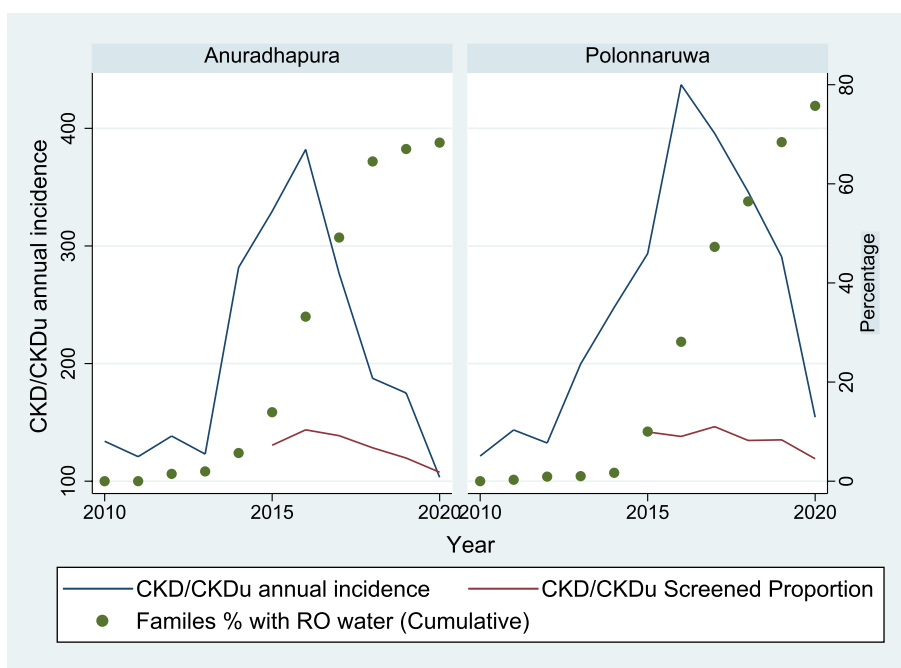


Fig. 1 The incidence of hospital diagnosed chronic kidney disease/chronic kidney disease of uncertain origin, screened proportion for chronic kidney disease/chronic kidney disease of uncertain origin and the percentage of families receiving reverse osmosis plant water from 2010 to 2020 in Anuradhapura and Polonnaruwa districts

CKD due to diabetes and hypertension takes a long time it is possible that there may be an increase in CKD rates in another 5 to 10 years time.

Most hypotheses for the causation of CKDu identified water as the medium of toxin entry into the human body [11]. This knowledge and poor accessibility to safe drinking water in the affected areas, led to acceleration of provision of safe drinking water to NCP by the government [15, 16]. The provision of community based drinking water RO plants commenced after 2011 in NCP [15, 16]. From 2010–2013 period 11 DS Divisions has commenced drinking water RO plant projects and in all of

these the decline in the incidence of hospital diagnosed CKD/CKDu occurred after more than 20% of the families received access to drinking RO water projects. The rest of 18 DS Divisions has commenced drinking water RO plant projects during 2014–2016 period and in 14 of these the decline in the incidence of hospital diagnosed CKD/CKDu occurred after more than 20% of the families received access to drinking RO water projects. In four DS divisions of Anuradhapura district decline begins well before reaching “20% family target” probably because these communities have started to access safe drinking water in different formats. Further these were CKD/

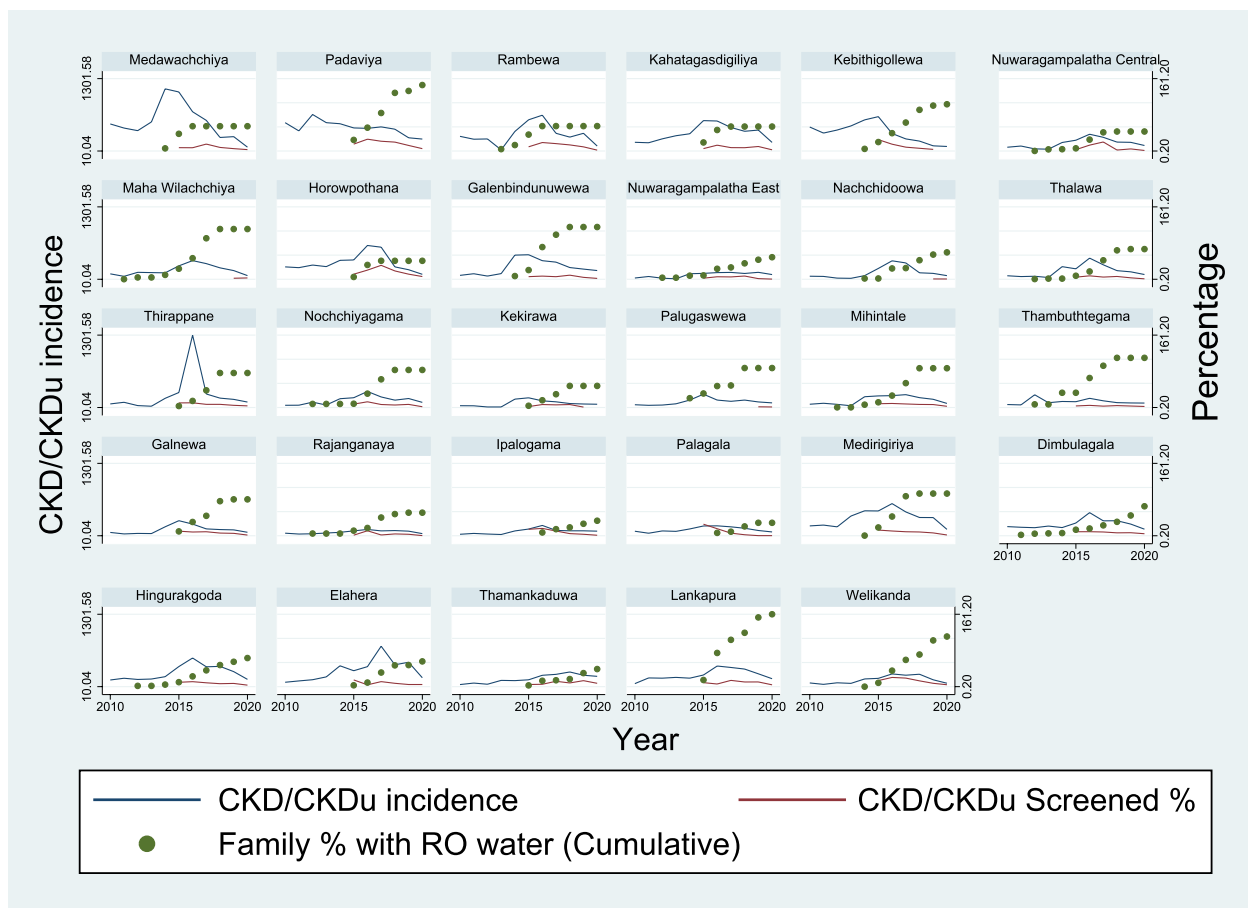


Fig. 2 The incidence of hospital diagnosed chronic kidney disease/chronic kidney disease of uncertain origin, screened proportion for chronic kidney disease/chronic kidney disease of uncertain origin and the percentage of families receiving reverse osmosis plant water from 2010 to 2020 in each DS division of North Central Province

CKDu low incidence areas (all four areas reporting the highest hospital diagnosed CKD/CKDu incidence rate of less than 215 per 100,000 population) and the residents were socio economically higher compared to other DS divisions. They may have started purchasing safe drinking water before commencement of drinking water RO plants. The initiation of community-based drinking water RO plants were late in these areas and also the number of coverage of drinking water RO plants are less in these areas probably indicating less requirement for community based water projects due to their accessibility to safe drinking water.

The coverage of families accessing drinking water RO plants exceeds 100% in some of the DS divisions as some families were accessing more than one drinking water RO plant.

In 2014 formal organized CKD/CKDu screening commenced in NCP. It is important to note that screening areas were priorities on the CKD/CKDu incidence. High proportions were screened in high incidence areas while

low proportions were screened in low incidence areas. The increase in the incidence of hospital diagnosed CKD/CKDu may be attributed to initiation of formal organized CKD/CKDu screening programmes, however the increase in the incidence continues even after the annual proportion being screened drops in most of the DS divisions, including the high incidence DS divisions. When comparing the annual screening rates from 2014–2016 period with 2017–2020 period there was no significant difference ($p=0.36$ in Anuradhapura district and $p=0.54$ in Polonnaruwa district) further indicating the trend in hospital diagnosed CKD/CKDu incidence not related to the CKD/CKDu annual screening rates. This concludes that there had been a general increase in the incidence of hospital diagnosed CKD/CKDu from 2013–2016 period and thereafter a rapid continuous decline. Thus, the screening rate and incidence of CKD/CKDu does not seem to have a relationship. Nevertheless, ascertainment bias exists since a direct comparison of hospital

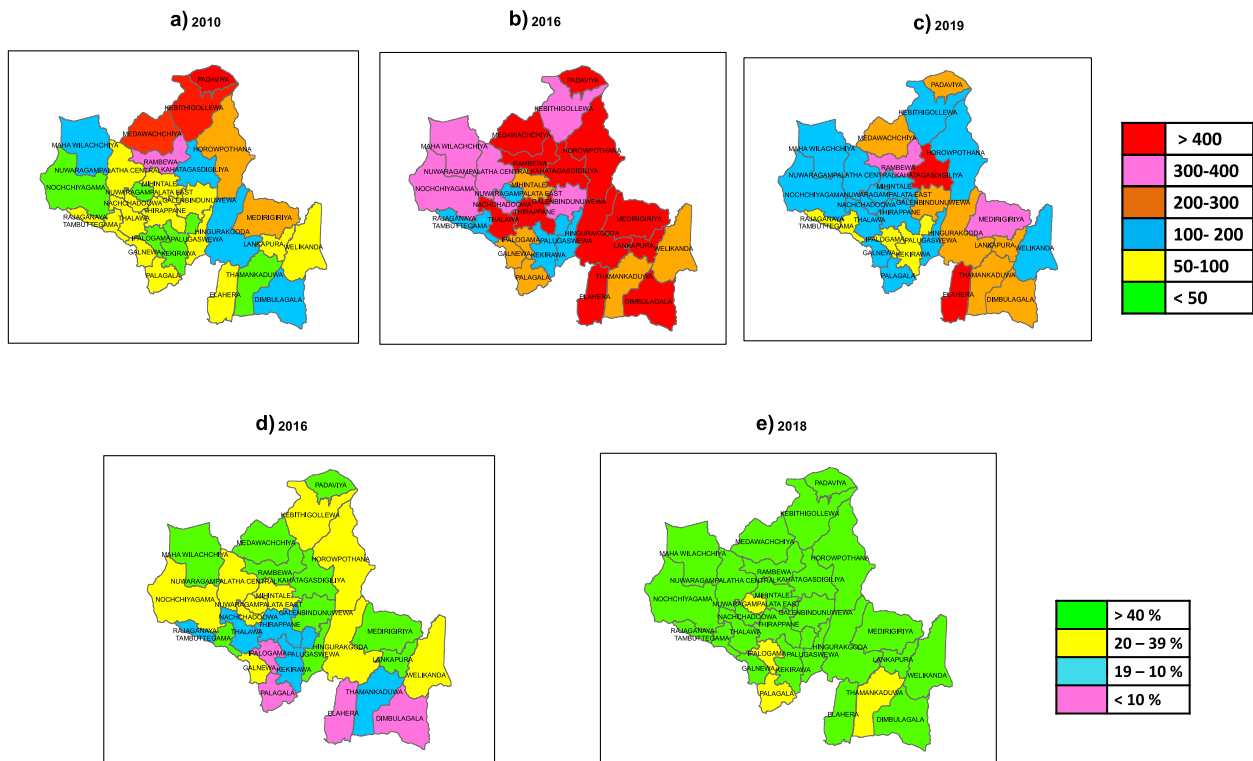


Fig. 3 The distribution of incidence of hospital diagnosed chronic kidney disease/chronic kidney disease of uncertain origin in North Central Province for the years (a) 2010, (b) 2016 & (c) 2019 and the availability of RO water in North Central Province for the years (d) 2016 and (e) 2018

diagnosed CKD/CKDu incidence with CKD/CKDu screened population is not possible.

There may be several reasons for the declining trend in hospital diagnosed CKD/CKDu incidence in NCP. Water may have been contaminated or there may have been some inherent factor which was causing the CKDu but aggravated by contaminated water. Thus, provision of safe drinking water may remove the risk of CKDu. Another hypothesis would be the provision of safe drinking water is palatable compared to hard water in the area thus an increase consumption of water due to palatability may have reduced the incidence of hospital diagnosed CKD/CKDu. At the same time, we also wish to draw attention to the fact that some putative nephrotoxins (paraquat, alachlor, chlorpyrifos, propanil and glyphosate) were banned in Sri Lanka from 2011 to 2015. When considering the implications of an environmental toxin, it is worth exploring the influence that this may have on the reduction in incidence of hospital diagnosed CKD/CKDu from 2016 onwards.

Presently the natural history of CKDu is poorly understood, although several theories have been proposed. These include heavy metals, agrochemicals, hardness of the water and cyanotoxins [3–10]. Majority of publications have indicated that the medium of transport for the

nephrotoxin is water [11]. Our findings support previous reportings [11, 27] indicating that provision of safe drinking water by supply of RO plants was associated with a decrease in the incidence of hospital diagnosed CKD/CKDu. However, if the nephrotoxin was transmitted by water, the relatively short period of 3.2 years taken to reduce the incidence is difficult to explain because the known mechanisms of renal damage due to nephrotoxins is often due to a chronic tubulointerstitial nephritis [28–30], which would have taken a longer period to reduce the incidence. Although not proven our explanation for this is as follows: The duration of the time taken to manifest the disease may depend on the concentration level of the nephrotoxin absorbed into the body. This may explain the geographical distribution of the disease incidence as the high disease incidence areas may have had a higher concentration of the nephrotoxin with the low incidence areas having a lower concentration. The accumulated nephrotoxin may require a threshold level to cause clinically manifest renal damage with different individuals having different threshold levels to cause the disease. Therefore, provision of safe drinking water midway during the pathogenesis of the disease may have prevented the threshold being reached in some susceptible individuals thereby reducing the incidence [11, 27].

Table 2 Incidence of hospital diagnosed chronic kidney disease/chronic kidney disease of uncertain origin, number screened for chronic kidney disease/chronic kidney disease of uncertain origin and the percentage of families provided with reverse osmosis water from 2010 to 2020 in Anuradhapura and Polonnaruwa districts

District/Division	Indicator	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Anuradhapura district	CKD/CKDu incidence	134.0	120.8	138.4	123.1	281.8	329.4	381.9	276.6	187.4	175.0	103.3
	% Families receiving RO water			1.5	2.0	5.7	13.9	33.2	49.2	64.5	67.0	68.3
Medawachchiya	No. Screened						62,427	89,184	79,051	57,957	40,172	15,586
	CKD/CKDu incidence	492.5	420.0	373.1	528.7	1119.3	1063.8	709.9	556.4	251.6	266.5	78.9
Padaviya	% Families receiving RO water					5.9	38.3	55.2	55.2	55.2	55.2	55.2
	No. Screened						3513	3420	7221	3753	2484	1479
Rambewa	CKD/CKDu incidence	587.0	417.4	756.6	587.0	565.3	478.3	469.6	500.0	452.2	273.9	247.8
	% Families receiving RO water						24.7	52.0	84.7	129.5	133.8	146.9
Kahatagasdigiliya	No. Screened						3525	6052	4998	4562	2854	1224
	CKD/CKDu incidence	304.5	244.7	250.1	24.5	405.1	647.1	742.2	367.0	288.2	367.0	103.3
Kebithigollewa	% Families receiving RO water				4.2	13.3	36.6	55.5	55.5	55.5	55.5	55.5
	No. Screened						3457	6946	6056	4992	3414	737
NPC (Nuwaragampalatha Central)	CKD/CKDu incidence	181.0	171.1	252.9	317.3	357.0	629.7	622.2	488.4	409.0	433.8	178.5
	% Families receiving RO water						19.1	46.8	54.4	54.4	54.4	54.4
Maha wilachchiya	No. Screened						2155	5240	3031	2976	4050	1090
	CKD/CKDu incidence	497.2	371.8	434.5	519.6	645.0	712.2	362.8	250.8	206.0	107.5	94.1
Horowpothana	% Families receiving RO water					4.8	19.9	39.7	63.4	91.7	101.2	104.1
	No. Screened						5645	3395	1914	1351	806	
Galenbindunuwewa	CKD/CKDu incidence	78.4	102.9	44.1	37.6	176.4	223.8	347.9	284.2	184.6	179.7	114.3
	% Families receiving RO water			0.4	3.8	4.2	6.2	25.6	41.7	43.6	43.6	43.6
NPE (Nuwaragampalatha East)	No. Screened						1975	8118	12,434	1444	2984	847
	CKD/CKDu incidence	106.8	62.3	133.5	129.8	124.6	249.3	342.7	289.3	213.6	164.7	75.7
Horowpothana	% Families receiving RO water					9.7	23.5	46.9	91.3	111.8	111.8	111.8
	No. Screened						400.1	700.2	665.0	256.8	197.4	102.7
Galenbindunuwewa	CKD/CKDu incidence	256.8	240.6	294.7	262.2	392	400.1	700.2	665.0	256.8	197.4	102.7
	% Families receiving RO water						5.1	31.9	41.1	41.1	41.1	41.1
NPE (Nuwaragampalatha East)	No. Screened						4186	7540	11,480	6860	4201	2234
	CKD/CKDu incidence	80.9	114.9	66.0	117.0	500.1	508.6	385.2	355.4	242.6	210.7	180.9
Horowpothana	% Families receiving RO water					7.1	20.5	71.7	99.3	116.3	116.3	116.3
	No. Screened						2716	3303	2712	4275	2016	887
Galenbindunuwewa	CKD/CKDu incidence	25.8	57.4	21.5	10.0	114.7	121.9	137.7	142.0	120.4	143.4	97.5
	% Families receiving RO water			3.5	3.5	8.0	8.6	23.3	26.4	35.5	43.5	49.1
NPE (Nuwaragampalatha East)	No. Screened						1724	3858	3617	5019	992	278

Table 2 (continued)

District/Division	Indicator	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Nachchidoowa	CKD/CKDu incidence	63.0	59.1	23.6	19.7	74.9	224.6	382.2	338.9	134.0	122.2	74.9
	% Families receiving RO water					1.7	1.7	24.1	24.9	42.4	55.0	59.9
Thalawa	No. Screened										168	152
	CKD/CKDu incidence	72.7	55.4	62.3	36.3	261.3	216.3	437.8	299.3	178.2	154.0	98.6
Thirappane	% Families receiving RO water			0.6	1.7	1.7	8.0	17.5	42.4	64.5	67.3	67.3
	No. Screened						2812	4523	2923	3706	1957	662
Nochchiyagama	CKD/CKDu incidence	74.0	103.5	44.4	33.3	173.8	277.3	1301.6	251.4	177.5	155.3	107.2
	% Families receiving RO water						3.3	14.7	38.2	76.9	76.9	76.9
Kekirawa	No. Screened						2771	2835	1899	1899	1307	980
	CKD/CKDu incidence	46.1	48.1	110.2	52.1	182.4	202.5	332.8	218.5	152.3	186.4	106.2
Palugaswewa	% Families receiving RO water			8.0	8.0	8.0	8.4	30.9	62.8	83.7	83.7	83.7
	No. Screened						3775	6385	3358	2761	3483	893
Mihintale	CKD/CKDu incidence	37.1	35.4	11.8	11.8	173.9	200.9	138.4	118.2	82.7	72.6	67.5
	% Families receiving RO water						3.9	16.1	29.6	48.1	48.1	48.1
Thambuthagama	No. Screened						1259	3928	3495	3928	558	
	CKD/CKDu incidence	57.8	44.9	51.3	77.0	154.0	276.0	154.0	128.4	154.0	115.5	96.3
Galnewa	% Families receiving RO water					20.7	31.2	47.8	49.1	87.9	87.9	87.9
	No. Screened										245	194
Rajanganaya	CKD/CKDu incidence	68.0	87.8	65.2	36.8	223.8	240.8	246.5	266.3	204.0	170.0	85.0
	% Families receiving RO water			0.4	0.4	6.3	11.6	26.5	54.3	87.5	87.5	87.5
Ipalogama	No. Screened						2962	3175	2774	2433	2321	957
	CKD/CKDu incidence	61.3	54.2	263.9	99.0	124.9	120.2	190.9	139.03	101.3	94.3	91.9
Galnewa	% Families receiving RO water			7.2	7.2	33.0	33.0	65.8	93.1	110.7	110.7	110.7
	No. Screened						1544	2122	1365	1903	1480	1100
Rajanganaya	CKD/CKDu incidence	69.1	43.2	51.8	48.9	169.8	279.1	218.7	132.4	120.8	115.1	71.9
	% Families receiving RO water						9.7	30.7	44.4	77.0	81.1	81.1
Ipalogama	No. Screened						3573	2904	3099	2088	1868	538
	CKD/CKDu incidence	53.7	35.8	41.7	56.6	71.6	101.4	131.2	101.4	107.3	95.4	44.7
Ipalogama	% Families receiving RO water			5.0	5.0	5.0	11.4	17.4	40.6	48.3	51.4	51.4
	No. Screened						455	3726	575	1363	1103	122
Ipalogama	CKD/CKDu incidence	30.9	48.9	36.0	25.7	100.4	139	213.6	110.6	102.9	102.9	95.2
	% Families receiving RO water						7.3	14.7	18.7	26.7	26.7	33.5
	No. Screened						5614	6366	4129	1875	1280	463

It has been reported that most of the drinking water in NCP is high in hardness and is not palatable resulting in poor hydration levels [12–14]. In fact, in Central America some studies have proposed chronic dehydration and heat stress as a possible mechanism which contributes to CKDu [31, 32]. If provision of palatable drinking water with the supply of RO plants resulted in better hydration of susceptible individuals in NCP of Sri Lanka, there is a possibility that provision of adequate hydration would have contributed to the reduction in incidence. It is also important to note that the regional health authorities of NCP publicised awareness programmes for consumption of safe drinking water which may have resulted in some individuals seeking access to safe drinking water even before community based RO plants were introduced [11, 17]. Although we have no data to support this hypothesis it may explain why the incidence decreased in a short period after introduction of RO plants.

The reduction of the hospital diagnosed CKD/CKDu incidence does not necessarily mean that the water is the transporter of the cause. The provision of safe drinking water probably resulted in a behavioral change in residents of CKDu affected areas to consume more water [15–17] which may have also reduced the risk for the disease. CKDu has also been reported in Central America [33], Andhra Pradesh in India [34], Tierra Blanca in Mexico [35], El-Minia Governorate in Egypt [36] and in Tunisia [37]. The arguments for the causation of CKDu in these areas are more or less similar compared to the Sri Lankan situation with high emphasis on contaminated water and occupational driven heat stress [38–41]. It would be noteworthy to assess the impact of provision of safe drinking water on incidence of CKDu in these areas.

Conclusion

In Anuradhapura and Polonnaruwa districts of NCP an increase in the incidence of hospital diagnosed CKD/CKDu was observed from 2010 to 2016 followed by a decreasing trend since 2017. Similar trend in the incidence of CKD/CKDu was seen in all DS divisions of Anuradhapura and Polonnaruwa districts as well. Provision of drinking water RO plants commenced in 2011 in NCP targeting CKD/CKDu high incidence areas. Continuous declining of hospital diagnosed CKD/CKDu incidence was observed after more than 20% of the families received access to drinking water RO plants in Anuradhapura and Polonnaruwa districts. This declining trend may be associated with provision of drinking water RO plants.

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Authors' contributions

AVR, APDS and CDS came up with the original idea. AVR, LCS, GWGP, RHK, APDS, JMCNG, SKCRK, MSFS, and CDS all helped to design the study and prepare the methodology. JMCNG, SKCRK and MSFS extracted the data from the secondary data sources. GWGP, RHK, APDS, JMCNG, SKCRK and MSFS did the analysis. AVR, LCS, GWGP, RHK, APDS, KGDS, JMCNG, SKCRK, MSFS, JSC and CDS all helped to interpret the data and write the manuscript. They all approved the final version and agreed to be accountable for all aspects of the work.

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Availability of data and materials

We have provided the raw aggregate data we used for analysis in Table 2, which is also available at the renal registry <https://nicst.com/iframe-renal-dev/>. The incidence information is also published in the Sri Lanka Annual Health Bulletin 2021. However, if anyone requires the same raw aggregate data they can be obtained from the National Renal Disease Prevention and Research Unit, Ministry of Health, Sri Lanka.

Declarations

Ethics approval and consent to participate

Not applicable.

The data used for this study are anonymised aggregated (routinely gathered) secondary data (personally identifiable data were not used). We have obtained this secondary data and conducted the analysis. During our study we have not come in contact with any patients for data gathering as anonymised secondary data were used, therefore consent was not sought since it was impossible to identify the individual persons. Therefore, ethical approval was not sought. All methods were carried out in accordance with relevant guidelines and regulations. Most of this data is also available in the Sri Lanka Renal Registry. The aggregate data is accessible to any persons. The approval for the study was obtained from the Ministry of Health, Sri Lanka.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Abeyssekera DTDJ, Kaiyoom SAA, Dissanayake SU. Place of peritoneal dialysis in the management of renal failure patients admitted to General Hospital Kandy. In: Kandy Society of Medicine 18th Annual Academic Conference. 1996.
2. Ranasinghe AV, Kumara GWGP, Karunaratna RH, et al. The incidence, prevalence and trends of Chronic Kidney Disease and Chronic Kidney Disease of uncertain aetiology (CKDu) in the North Central Province of Sri Lanka: an analysis of 30,566 patients. *BMC Nephrol.* 2019;20:338.
3. Jayatilake N, Mendis S, Maheepala P, Mehta FR. Chronic kidney disease of uncertain aetiology: prevalence and causative factors in a developing country. *BMC Nephrol.* 2013;14:180.
4. Jayasumana C, Gunatilake S, Senanayake P. Glyphosate, hard water and nephrotoxic metals: are they the culprits behind the epidemic of chronic kidney disease of unknown etiology in Sri Lanka? *Int J Environ Res Public Health.* 2014;11:2125–47.

5. Jayasumana C, Gajanayake R, Siribaddana S. Importance of arsenic and pesticides in epidemic chronic kidney disease in Sri Lanka. *BMC Nephrol*. 2014;15:124.
6. Chandrajith R, Nanayakkara S, Itai K, et al. Chronic kidney diseases of uncertain etiology (CKDu) in Sri Lanka: geographic distribution and environmental implications. *Environ Geochem Health*. 2011;33:267–78.
7. Wanigasuriya KP, Peiris-John RJ, Wickremasinghe R. Chronic kidney disease of unknown aetiology in Sri Lanka: is cadmium a likely cause? *BMC Nephrol*. 2011;12:32.
8. Herath C, Jayasumana C, De Silva PMCS, De Silva PHC, Siribaddana S, De Broe ME. Kidney diseases in agricultural communities: A case against heat-stress nephropathy. *Kidney Int Rep*. 2018;3:271–80.
9. Manage PM. Cyanotoxins: A hidden cause of chronic kidney disease of unknown etiology (CKDu) in Sri Lanka – A review. *Sri Lanka J Aquat Sci*. 2019;24(1):1–10.
10. Ranasinghe HRALN, Lokuge LDMN, Edirisinghe JC, Bandara L. Water treatment, preventive measures and the chronic kidney disease in the farming community in Sri Lanka. *J Agric Sci-Sri Lanka*. 2015;10:98–108.
11. De Silva MWA. Drinking water and CKD of unknown etiology in Sri Lanka: A community perspective. *Ann Nutr Metab*. 2020;76(suppl 1):37–42.
12. Imbulana S, Oguma K, Takizawa S. Evaluation of groundwater quality and reverse osmosis water treatment plants in the endemic areas of Chronic Kidney Disease of Unknown Etiology (CKDu) in Sri Lanka. *Sci Total Environ*. 2020;745:140716.
13. Cooray T, Wei Y, Zhong H, Zheng L, Weragoda SK, Weerasooriya R. Assessment of groundwater quality in CKDu affected areas of Sri Lanka: implications for drinking water treatment. *Int J Environ Res Public Health*. 2019;16(10):1698.
14. Wimalawansa SJ. Effect of water hardness on non-communicable diseases, including chronic kidney disease of multifactorial origin (CKDmfo/CKDu). *J Environ Health Sci*. 2016;2(1):1–11.
15. Imbulana S, Oguma K, Yakizawa S. Evaluation of ground water quality and reverse osmosis water treatment plants in the endemic areas of chronic kidney disease of unknown etiology (CKDu) in Sri Lanka. *Sci Total Environ*. 2020;745:140716.
16. Horbulyk T, Kafle K, Balasubramanya S. Community response to the provision of alternative water supplies: A focus on chronic kidney disease of unknown aetiology (CKDu) in rural Sri Lanka. *Water International*. 2021;46(1):37–58.
17. De Silva MWA. Drinking water and chronic kidney disease of unknown aetiology in Anuradhapura. *Sri Lanka Anthropology & Medicine*. 2019;26(3):311–27.
18. Levey AS, Eckardt KU, Tsukamoto Y, et al. Definition and classification of chronic kidney disease: a position statement from kidney disease: improving global outcomes (KDIGO). *Kidney Int*. 2005;67:2089–100.
19. Levey AS, Stevens LA, Schmid CH, Zhang Y, Castro A III. New equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150(9):604–12.
20. World Health Organization. Expert Consultation on Chronic Kidney Disease of Unknown Etiology. 2016.
21. Palihawadana P, Hewage R, Maathu S, et al. Screening Guidelines, Chronic Kidney Disease of Sri Lanka 2017. 2nd ed. Colombo: Epidemiology Unit, Ministry of Health; 2017.
22. Census of Population and Housing of Sri Lanka 2011. Colombo: Department of Census and Statistics. 2012.
23. Ruwanpathirana T, Senanayake S, Gunawardana N, et al. Prevalence and risk factors for impaired kidney function in the district of Anuradhapura, Sri Lanka: a cross-sectional population-representative survey in those at risk of chronic kidney disease of unknown aetiology. *BMC Public Health*. 2019;19:763.
24. Rannan-Eliya RP, Wijemunige N, Perera P, et al. Prevalence of diabetes and pre-diabetes in Sri Lanka: a new global hotspot—estimates from the Sri Lanka Health and Ageing Survey 2018/2019. *BMJ Open Diab Res Care*. 2023;11:e003160.
25. Senanayake S, Ruwanpathirana T, Gunawardana N. Hypertension in a rural community in Sri Lanka: prevalence, associated factors and its effect on the renal profile. *J Hypertens*. 2019;37(9):1805–12.
26. Athuraliya TN, Abeysekera DT, Amerasinghe PH, Kumarasiri PV, Disanayake V. Prevalence of chronic kidney disease in two tertiary care hospitals: high proportion of cases with uncertain aetiology. *Ceylon Med J*. 2009;54(1):23–5.
27. Bu LK, Jia PP, Li WG, Li YZ, Li TY, Pei DS. Probiotics mitigate kidney damage after exposure to Sri Lanka's local groundwater from chronic kidney disease with uncertain etiology (CKDu) prevalent area in zebrafish. *Aquat Toxicol*. 2023;262:106671.
28. Athuraliya NT, Abeysekera TD, Amerasinghe PH, et al. Uncertain etiologies of proteinuric-chronic kidney disease in rural Sri Lanka. *Kidney Int*. 2011;80(11):1212–21.
29. Nanayakkara S, Komiya T, Ratnatunga N, et al. Tubulointerstitial damage as the major pathological lesion in endemic chronic kidney disease among farmers in North Central Province of Sri Lanka. *Environ Health Prev Med*. 2012;17:213–21.
30. Nanayakkara S, Senevirathna ST, Karunaratne U, et al. Evidence of tubular damage in the very early stage of chronic kidney disease of uncertain etiology in the North Central Province of Sri Lanka: a cross-sectional study. *Environ Health Prev Med*. 2012;17:109–17.
31. Glaser J, Lemery J, Rajagopalan B, et al. Climate change and the emergent epidemic of CKD from heat stress in rural communities: the case for heat stress nephropathy. *Clin J Am Soc Nephrol*. 2016;11:1472–83.
32. Roncal-Jimenez C, Lanasa MA, Jensen T, Sanchez-Lozada LG, Johnson RJ. Mechanisms by which dehydration may lead to chronic kidney disease. *Ann Nutr Metab*. 2015;66(suppl 3):10–3.
33. Ramirez-Rubio O, McClean MD, Amador JJ, Brooks DR. An epidemic of chronic kidney disease in Central America: an overview. *J Epidemiol Community Health*. 2013;67:1–3.
34. Abraham G, Agarwal SK, Gowrishankar S, Vijayan M. Chronic kidney disease of unknown etiology: hotspots in India and other Asian countries. *Nephrol*. 2019;39(3):272–7.
35. Madero M, Aguilar D, Rana A, Escobar A, Villa A, Obrador G. Decreased kidney function among rural population in Tierra Blanca Mexico: a cross-sectional study. *J Am Soc Nephrol*. 2017;28:529.
36. El Minshawy O. End-stage renal disease in the El-Minia Governorate, upper Egypt: an epidemiological study. *Saudi J Kidney Dis Transpl*. 2011;22(5):1048–54.
37. Hassen W, Abid S, Achours A, Maaroufi K, Creppy EE, Bacha H. Ochratoxin A and human nephropathy in Tunisia: a ten years survey *Annales de Toxicologie*. 2003;15(1):21–9.
38. Pearce N, Caplin B. Let's take the heat out of the CKDu debate: more evidence is needed. *Occup Environ Med*. 2019;76(6):357–9.
39. Wesseling C, Glaser J, Rodríguez-Guzmán J, et al. Chronic kidney disease of non-traditional origin in Mesoamerica: a disease primarily driven by occupational heat stress. *Rev Panam Salud Publica*. 2020;44:e15.
40. John O, Gummudi B, Jha A, et al. Chronic Kidney Disease of Unknown Etiology in India: What Do We Know and Where We Need to Go. *Kidney Int Rep*. 2021;6(11):2743–51.
41. Campese VM. The unresolved epidemic of chronic kidney disease of uncertain origin (CKDu) around the world: a review and new insights. *Clinical Nephrology*. 2021;95(2):65.

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