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## Original Article

# Factors Associated with Chronic Kidney Disease of Unknown Aetiology among the Patients who Seek Treatment from the Nephrology Clinic of General Hospital –Vavuniya

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## Abstract

Chronic Kidney Disease of unknown aetiology (CKDu) is one of the major health care problems in Sri Lanka. This community-based case-control study was conducted to identify potential causes of CKDu. The study also designed to identify suspected CKDu causative based on social-cultural factors and water quality parameters among the patients who sort treatment from the General Hospital (GH), Vavuniya Nephrology Clinic.

The case group consisted of 106 patients who have CKDu and sort treatment from the nephrology clinic at GH Vavuniya. The control group consisted of 100 people who willingly participated and lived in the vicinity of the patient houses, and had not reported kidney disease (confirmed by screening program of CKD unit). The water samples were collected from their drinking water source which was used for more than five years before having diagnosed with CKDu.

The data was analysed using chi-square with cross-tabulation. On the comparison between the CKDu group and the control group, a significant correlation was observed for smoking “Beedi”, engaging in farming, low level of education, and exposure to weedicides. In the analysis of water quality parameters, colour and electrical conductivity were elevated. However there was no single water quality parameter that could clearly and directly be related to the aetiology of CKDu, however, it was found that the colour, and electrical conductivity of water samples were higher than that of WHO recommendations.

**Keywords :** CKDu, Water quality parameters, Social and cultural habits, Weedicide.

## Introduction

Chronic kidney disease of unknown etiology (CKDu) was first reported in 1994 among paddy farmers in the Padaviya farming area in the North Central Province (NCP) of Sri Lanka (Jayasumana et al., 2013; Jayasumana et al., 2013). Twenty years after the first report, CKDu is one of the major health concerns in Sri Lanka today, with more than 50,000 estimated patients in the North Central province, and spreading on an epidemic scale to other farming areas in the Northern, North-Western, Central, Uva and Eastern provinces of the country (Redmon et al., 2014). Previous studies, indicated that the incidence of CKDu in Sri Lanka has been doubling every four to five years so that currently more than 150,000 people are affected by the disease and about 3% deaths are reported annually (Wimalawansa & Wimalawansa, 2014). The high cost involved in the management of end-stage renal failure has led to a substantial burden on health care resources.

It is a hypothesis that CKDu in Sri Lanka maybe associated with environmental factors (Gunatilake, Samaratinga, & Rubasinghe, 2014). CKDu in Sri Lanka may be attributed to irrigation work and fertilizer runoff from agricultural regions. Dharmawardana et al., 2014, suggested that CKDu may be due to pollutants and toxins ingested from food, direct ingestion of toxins when handling agrochemicals, and prolonged exposure to toxins and pollutants from drinking water (Dharmawardana, Amarasiri, Dharmawardene, & Panabokke, 2015). It was further proposed that prolonged consumption of drinking water with high ionicity affects the kidney membrane adversely. There are several examples to support these suggestions. The Cadmium toxicity of people living in the Jinzu river basin, Japan, in the 1950s was due to a commercial discharge from mine contaminating water used for drinking and due to irrigation of paddy (Wanigasuriya, 2012). Chinese herbal nephropathy which is a form of intestinal nephritis was first reported in 1994 and Belgium women who had undergone slimming therapy with Chinese herbs containing aristolochic acid presented with interstitial nephritis. The Balkan endemic nephropathy (BEN) which was first described in 1956 was found to be associated with dietary exposure to aristolochic acid (AA) which caused cancer (Wanigasuriya, 2012).

Epidemics of CKDu are also reported in other different regions of the world, including areas of India and Central America (Agampodi, Amarasinghe, Naotunna, Jayasumana, & Siribaddana, 2018)

Similar issues were identified among rice farmers in Sri Lanka. Further a similar disease condition was reported among sugarcane plantation workers in Nicaragua and El Salvador in Central America. Both diseases demonstrated clinicopathological similarities and are also referred to as Chronic Interstitial Nephritis in agricultural communities (CINAC) (Jayasumana et al., 2017). More recently similar forms of CKDu have been identified in Andhra Pradesh in South India (Ruwanthirana et al., 2019).

This study aims to assess the parameters which affect the CKDu in Vauniya and to assess the water quality parameters

that might have had an impact on CKDu.

## Methodology

### Study Design

This study was a case-control study conducted in the Vavuniya district. 350 patients attending the Nephrology clinic of GH Vavuniya receiving treatment for CKDu were enrolled in the study. Informed consent was obtained from each participant who volunteered to participate after explaining the nature of the study.

### Study Population and Sampling Method

For the study 106 patients were randomly selected from 350 CKDu patients. Water samples were collected from home visits of all 106 patients. One hundred people who volunteered and lived in the vicinity and had not reported kidney disease were selected as the control group, (Confirmed by screening program of CKD unit).

An interviewer-administered questionnaire was used to collect information on demography, health status, details of the drinking water source, food habits, etc.

### Sample Size

The sample size was calculated by Kelsey formula for case-control studies in OpenEpi software version 3.1 with  $\alpha = 0.05$ , power = 80, the ratio of cases to controls = 1.0, the hypothetical proportion of exposure among controls = 50, and an odds ratio (OR) of 2 as a minimum difference between groups to be detected.

### Inclusion criteria

Patients with CKDu who sort medical treatment from GH Vavuniya, (where most of the CKDu patients live in North and North-Central Province)

### Exclusion criteria

CKDu due to, diabetes type 1 and 2, hypertension, immune system diseases (Lupus nephritis), long-lasting viral illnesses, such as HIV/AIDS, hepatitis B, and hepatitis C, pyelonephritis, urinary tract infections, polycystic kidney disease, congenital defects of kidneys, drugs/ toxins/ lead poisoning and long-term use of some medications including NSAIDs (nonsteroidal anti-inflammatory drugs)

### Study Instrument

The questionnaire and data collection sheet were used as the study instruments. Parameters of the water samples were measured using water analyzer DR6000. The water quality parameters such as, pH, total dissolved solvent (TDS), electrical conductivity, and turbidity were measured using the respective meter

### Sample collection and preparation

Water samples of the drinking water source of each participants (which have been used for more than 5 years before being diagnosed with CKDu) were collected into

1000ml volume plain, plastic bottles, and sent to the laboratory without delay (without any preservatives). The water samples were analyzed within six hours after collection.

### Ethical Clearance

Ethical approval for the study was obtained from the ethics review committee of KIU (KIU/ERC/18/048). Further approval was obtained from the Director of the Vavuniya General Hospital.

## Results and Discussion

In the CKDu population 85 (80.2%) were males and 21 (19.8%) were females compared to the control group with 68 (86%) males and 32 (32%) female. Majority of the CKDu and control population were married (102, 96.2% and 90, 90% respectively). The median age of both groups was 60 years.

Majority of the CKDu population had attended school up to grade 8 (52, 49.1%) but only two individuals had studied up to postgraduate level. Similarly, three individuals in the control group had also possessed postgraduate qualifications. There were no drastic differences between the education level among test and control group (Table 1).

Table 1- Education level in the test and control group

Educational level	CKDu group (n=106)		Control (n=100)	
	Number	%	Number	%
No schooling	19	17.9	6	6
Up to grade 8	52	49.1	42	42
Up to O/L	29	27.4	23	23
Up to A/L	4	3.8	16	16
Graduate	0	0	10	10
Post Graduate	2	1.9	3	3

When the occupations of the individuals enrolled in the study were investigated, it could be observed that majority of the CKDu population were occupied in farming (26, 24.5%) and in agricultural labouring (26, 24.5%) (Table 2).

Table 2- Occupations of test and control groups

Socio Demographic Factor	CKDu group (n=106)		Control (n=100)	
	N	%	N	%
Occupation				
Farmers	26	24.5	20	20
Agricultural labourer	26	24.5	12	12
Businessmen	6	5.7	12	12
Management Assistant	9	8.5	6	6
Teachers	0	0	11	11
Housewife	9	8.5	25	25
Fishermen	1	1	4	4
Other occupation	38	35.8	10	10

Out of 106 CKDu patients, 52 had occupations related to farming (Farmers and agricultural laborers). The results of the chi square test showed that there is a significant association between CKDu and occupations associated with farming ( $p=0.001$ ).

Table 3. Association of CKDu with behavioural and environmental factors

	CKDu		Control		P value
	Yes	No	Yes	No	
Smoking beedi	18	88	2	98	<0.001
Consumption of alcohol	16	90	13	87	0.693
Chewing betel	17	89	17	83	0.852
Exposure to weedicides	21	85	0	100	0.001

Using weedicides and smoking beedi have also shown significant association with CKDu (table 3). Exposure to weedicides maybe prevalent in individuals who have occupations associated with farming which maybe one of the reasons that farming shows a significant association with CKDu.

Studies conducted to determine the causative factors of CKDu have reported that agrochemicals maybe one of the leading factors in the development of this disease. (Jayasumana et al., 2013; Jayatilake, Mendis, Maheepala, & Mehta, 2013; Peiris-John, Wanigasuriya, Wickremasinghe, Dissanayake, & Hittarage, 2006). Further Jayasumana et al., (2013) also reported that pesticides and fertilizers which are excessively used in paddy farming may be a likely source of arsenic in CKDu patients in the study area (Jayasumana et al., 2015; Jayasumana et al., 2013). However Ruwanpathirana, in 2019, revealed that particular exposures associated with farming (e.g. pesticide exposure, heat exposure) did not appear to explain the increased risk of CKDu, due to limited available information (Ruwanpathirana et al., 2019). Thus the reasons for high CKDu prevalence still remains an enigma.

There are very few number of research published on beedi consumption and associated health risks in Sri Lanka. A report published by Alcohol and Drug Information Centre in 2014 has identified beedi as a cheap form of tobacco with a large consumer base mostly in rural areas (ADIC, 2014). However the risks associated with beedi consumption has not been properly investigated and the government restriction on cigarettes may have increased the consumption of beedi (Gunasinghe, 2018). Smoking beedi maybe a habitual behavior of some individuals involved in farming, however more research maybe needed to identify the underlying risks which may relate to the development of CKDu.

The water quality parameters measured from the water samples collected from the water sources used by the CKDu patients and controls are mentioned in table 4. The average of the most water quality parameters did not exceed the WHO recommendation and national recommended values in any of the sampling groups. However, the colour of the water sample and electrical conductivity were elevated compared to the standards. Therefore, further research should be carried out to find factors affecting the colour of the water samples and electrical conductivity.

Table 4-Summary water quality parameters.

Water quality parameters	Mean (CKDu)	Mean (Control)	SLS 614: 2013 recommendation	WHO Recommendation
Colour (Hazen)	20.11	16.43	15	2
Turbidity (NTU)	0.49	0.54	2	<1
pH at 25°C	7.08	7.1	6.5 - 8.5	6.5-8.5
TDS (mg/L)	488.21	464.78	500	1,000
NO <sub>3</sub> <sup>-</sup> (mg/L)	1.52	1.33	50	50
NO <sub>2</sub> <sup>-</sup> (mg/L)	0.04	0.03	3	3
F <sup>-</sup> (mg/L)	0.34	0.45	1	1.5
PO <sub>4</sub> <sup>-3</sup> (mg/L)	0.59	0.63	2	-
Fe (mg/L)	0.10	0.06	0.3	0.1
SO <sub>4</sub> <sup>-2</sup> (mg/L)	36.17	32.28	250	
Electrical conductivity(μS/cm)	979.22	891.54	<400	

## Conclusion

Occupations associated with farming maybe at a higher risk of developing CKDu in the study population. Factors that may also contribute to the risk of developing CKDu maybe the use of weedicides and habit of smoking beedi.

The quality of water may also affect the development of CKDu but further investigations maybe needed to isolate the specific parameters.

## Future recommendations

It is recommended to conduct further surveys in other districts of the country using the same protocol to study the prevalence and causative factors of suspected CKDu for better understanding.

Due to the limited facilities available, samples had to be analysed only for a few chemical parameters. But it is important to study further water quality parameters of the water samples from several areas of the country.

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## Conflicts of interest.

There are no conflicts of interest.

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