Original Article

Prevalence of Chronic Kidney Disease and its Association with Pesticide Exposure in Bargarh District, Odisha, India

Abstract

Background: Bargarh, a district in Odisha, is known for intense agricultural activities because of uninterrupted irrigation from the Hirakud reservoir. The number of chronic kidney disease (CKD) cases in the district is increasing rapidly. The present study assesses the prevalence of CKD and CKDu (of unknown etiology) in the district and its association with pesticide application. **Materials and Methods:** A door-to-door survey was conducted to find out the CKD hotspots in the different blocks of the district with the help of primary and community health centers. The prevalence of CKD in the identified hotspot villages was assessed using a random clustered sampling method along with the collection of data related to age, sex, occupation and source of drinking water. Soil and water samples collected from identified hotspot and nonhotspot villages were analyzed to assess the presence of nephrotoxic pesticide residues. **Results:** A total of 16 villages were identified with high CKD prevalence rates and designated as hotspot villages. Data indicate that about 21% of males under ≥ 40 years age group were found to be suffering from CKD. Cases of CKDu (85%) were more prominent in these hotspot villages. Analysis of soil and water samples demonstrated the presence of seven different nephrotoxic pesticides above the maximum residues levels (MRLs) in hotspot villages compared to nonhotspot villages. **Conclusion:** The presence of nephrotoxic pesticides above MRLs in the hotspot villages indicates their possible association with the onset and progression of CKD among the exposed population. Further research is needed to establish their causative association with CKDu in the study region.

Keywords: *CKD prevalence, Bargarh district, Odisha, Pesticide, Community based survey*

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Introduction

The last quarter century witnessed significant global population growth, aging, and an accelerated pace of epidemiologic transition, with reduced mortality from communicable diseases and an increased burden of noncommunicable diseases.[1] Over the years, chronic kidney disease (CKD) has emerged as a major public health problem and a significant contributor to the overall noncommunicable disease burden globally,[2,3] which accounts for nearly 700 million active cases and 1.2 million deaths per year (GBD Chronic Kidney Disease Collaboration 2020). Worldwide, the prevalence of CKD varies from 8% to 16% representing over 750 million cases. Of which 78% (387.5 million) are from low- to middle-income countries.[3,4] According to the systematic analysis of the global burden of diseases, CKD contributes significantly to global morbidity and also as a risk factor for cardiovascular diseases.[5] The number of adults living with diabetes quadrupled between 1980 and 2014, increasing from 108 million in 1975 to 1.13 billion in 2015.[6] The primary cause of CKD is diabetes and hypertension, especially in developed countries.[7] However, for more than two decades, various regions of the world have experienced an excess of CKD unrelated to these traditional causes, referred to as "CKDu," particularly in Central America and Mexico (Mesoamerican nephropathy),[8] the North-Central Province of Sri Lanka[9,10] and in the state of Andhra Pradesh of India[11] (Uddanam endemic nephropathy), and Supebeda Chattisgarh[12] and possibly in other countries like Egypt,[13] Tunisia and Morocco,[14] and Saudi Arabia.[15]

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Based on experimental and clinical evidence, a number of pesticides in common use in many parts of the globe are known human nephrotoxins, causing chronic kidney disease (CKD) and acute kidney injury (AKI). Triple super phosphates and rock phosphates are extensively used in agriculture in the dry zone are found to be rich in toxic heavy metals like Cd, As, Cr, Co, Ni, Hg, Pb, V, and U.[9,16,17] Pesticide residues such as 2, 4-dichlorophenoxyacetic acid (2,4D), pentachlorophenol (PCP), chlorpyrifos, carbaryl naphthalene, glyphosate, paraquat, and amino methyl phosphonic acid (AMPA) were detected in biological samples of CKDu patients, and some of them exceed the reference level suggested by WHO. The first CKDu review published from India recommended investigating, besides silica and heat stress, also pesticides as potential etiologies.[18] The regional nephropathies occur mostly in poor adult workers in hot tropical agricultural areas, more frequently among males than in females. The most paramount causes for CKDu are occupational stress, exposure to heat stress,[19,20] chemicals, and pesticides.[21] Side effects of some medicines commonly used can also contribute toward the CKDu. However, a detailed quantitative analysis of the global, regional, and national burden of CKD over the past 25 years is not available. During the recent years, there have been increasing reports of CKD cases from the State of Odisha, India. Only, limited research exploring the contributing factors from this region is available.[22]

With the commissioning of the Hirakud Dam, Bargarh and its adjacent area became the rice bowl of the state due to the availability of fertile land and uninterrupted irrigation facilities. A large population of the district depends upon agricultural activities as their major source of income. A total of 348747 hectares in the district comes under cultivated land. Sixty-five% of the cultivated land is fully irrigated under the Hirakud Dam irrigation command region. Paddy is the major crop grown in this area with extensive use of agrochemicals in the district. The prevalence of CKD and CKDu cases in this region has not been investigated. The present study attempts to estimate the burden of CKD and CKDu in different parts of Bargarh districts. The study also investigates the association of pesticide exposure in inducing nephropathy among the people of Bargarh district, Odisha, India.

Materials and Methods

The study was conducted at Bargarh district located at 21.33°N, 83.62°E, having a total geographical area of 5837 km^2. As per census reports (2011), the district has a total population of 1,481,255 of which the male population constitute 7,49,161 and female of 7,32,094. The district is divided into 12 different blocks. Agriculture is the major occupation of the majority of the populace. Around 60% of the cultivated land of the district is under irrigation by Hirakud Dam Command. Paddy is the most prominent crop cultivated in this region.

The study was approved by the Institutional Ethics Committee of Sambalpur University under the supervision of Veer Surendra Sai Institute of Medical Science and Research, Burla, Odisha vide letter, number 189-2022/I-F-O/79, dated 05.08.2022. A cross-sectional study was undertaken in 16 selected hotspot villages of Bargarh district coming under four blocks using clustered random sampling technique and probability proportionate to size (PPS) methodology. The population is divided into clusters, where cluster villages were heterogeneous with respect to socioeconomic status, occupation, age, level of education, and all the clusters selected fall under an intensive agricultural zone that shares homogeneity between the clusters. All the clusters were assigned with a unique identifier followed by a lottery to ensue randomization. A total of 2109 individuals were screened from 16 clusters (villages) selected in the defined study area. Among the screened population 1083 were males and 1026 were females' participants, the average age of the whole population screened was found to be 54±11.22 (SD).

Determination of CKD prevalence in the district

A door-to-door survey was conducted. Sixteen villages in five blocks of Bargarh district, that is eight from Bijepur, two from Gaisilate, one from Bheden, three from Attabira, and two from Bhatli, were designated as hotspots for CKD/CKDu cases having the incidence of CKD prevalence $>1\%$ [Figure 1].

Random clustered sampling of the population in designated CKD hotspot villages was carried out to determine the CKD prevalence. Other parameters such as prevalence of hypertension, diabetes mellitus (DM), gender, age, occupation, address, and source of drinking water were collected using a predesigned proforma.

Arm blood pressure was measured after 5 minutes of rest in the sitting position using an automated clinically validated sphygmomanometer (Dr Morpen, Model- BP 15, India). An average of three readings was recorded. Height and weight were measured using a stadiometer (SECA model 213, Hamburg, Germany) and digital calibrated scales (OMRON Model HN 865).

Prior to the collection of blood samples, consent from the participants was obtained using a standard informed concern form. A blood sample (10 ml) was collected from the peripheral veins using plain tubes and fluoride tubes from each participant. The collected blood samples were transported in an ice-carrier to Regional Diagnostic Centre, Veer Surendra Sai Institute of Medical Sciences and Research, Burla, Odisha, for further laboratory analysis. The blood samples were processed on the same day of sample collection. Serum samples were separated immediately by centrifugation at 3000 rpm for 10 minutes. Random blood

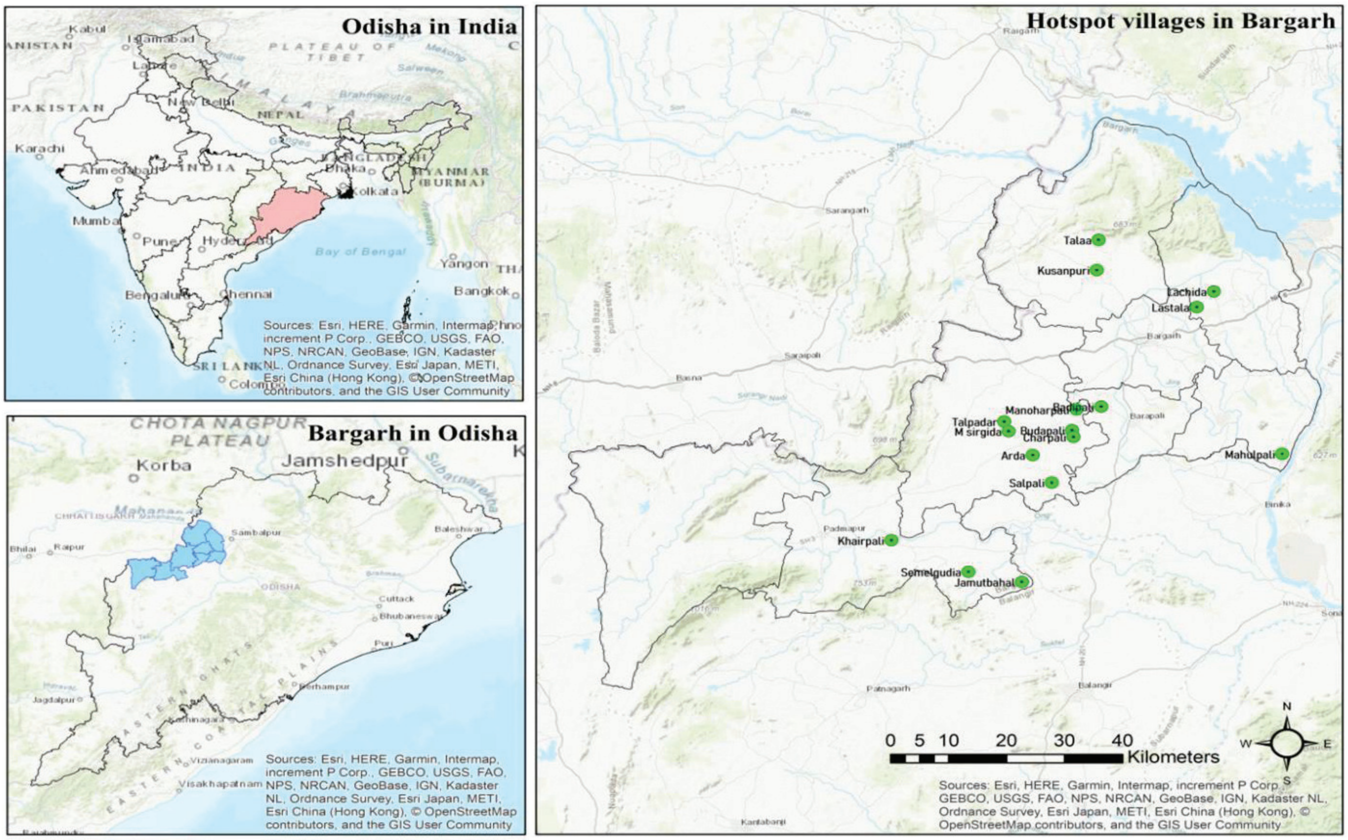

Figure 1: Map showing the hotspot villages of Bargarh district, Odisha, India.

sugar and serum creatinine were estimated and carried out using the Transasia XL 1000 Auto Analyzer.

First morning void urine samples (5 ml) were collected from all the patients in polypropylene urine collection bottles, the samples were stored in an ice box (4^{o}C) and transported to the lab where the sample was analyzed for proteinuria using a heat coagulation test and corrected for creatinine.

Reagents and standards

Glass-fiber filters (0.45 μm) and needle-type nylon membrane (0.22 μm, GE Healthcare) used in removing particulate matter before chromatographic analysis were procured from GE Healthcare, USA. Mixtures of 16 and 25 pesticide analytes were prepared in hexane for gas chromatography–mass spectrometry (GC–MS) and acetonitrile for ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS).

Estimation of pesticide residues in water and soil samples

Topsoil (10–15 cm depth) samples were collected from agricultural land from all the identified 16 hotspot villages and from 10 nonhotspot villages of Bargarh district. The soil samples were air dried, powdered, and passed through a mesh of 2 mm. Twenty-gram soil samples in triplicate were taken in 100 mL polypropylene centrifuge tubes. The collection of water samples was performed from ponds, canals, and rivers of all the selected hotspot and nonhotspot villages. A total of 120 water samples were collected from different sites. Grab sampling was done, and samples were collected in one-liter amber-colored glass bottles. The samples were transported in cool box with ice packs. After transportation to the laboratory, samples were stored at 4°C, and extraction was mostly done within 48 h.

The topsoil extraction was carried out using a modified QuEChERS method coupled with ultrasound-assisted extraction.[23,24] Soil sample (10 g) was mixed with acetonitrile and acidified deionized water and extracted ultrasonically for 20 min. The extracts were centrifuged at 3000g for 10 min and the organic phase was collected. The organic phase was then evaporated with a vacuum rotary evaporator. The extracts were re-dissolved to 6.0 mL by acetonitrile and then divided into two aliquots. Aliquots of 3.0 mL were evaporated to near dryness at 40°C with a rotary evaporator[25] and reconstituted with 1 mL methanol for UPLCMS/MS and 1 mL n-hexane for GC-MS, respectively.

For surface water samples, a 20 mL aliquot of the water sample was filtered through a 0.45-μm glass-fiber filter and then added to a glass conical bottle containing 20 mL acetonitrile acidified with 120 μL acetic acid. The extraction, purification, concentration, and chromatographic analysis were the same as the soil samples.

Diagnostic criteria and definition for CKD and CKDu

The diagnostic criteria followed for identifying patients with CKD are diseases persisting for more than 3 months, glomerular filtration rate (eGFR) < 60 ml/min/1.73 m^2; albuminuria or proteinuria, urine albumin excretion ≥30 mg/d or albumin to creatinine ratio ≥30 mg/mmol, and urine sediment abnormality showing isolated microscopic hematuria with dysmorphic RBCs. Hypertension was defined as blood pressure more than 140/90 mm Hg. Diabetes was defined as fasting blood glucose >126 mg/dl or random blood glucose >200 mg/dl or on any medication for diabetes. The patients with a history of prolonged hypertension, diabetes, and other known etiologies were categorized as the CKD group. All other CKD cases with no history of diabetes or hypertension or have mild hypertension, protein creatinine ratio (PCR) ≤1, restricted to a specific geographical location, predominance among younger males and people of the low-income group mostly working in an extreme environmental condition such as extreme heat, and dehydration and with progressive end-stage renal failure, were included under CKD with unknown etiologies (CKDu).[26]

Statistical analysis

Data were analyzed using IBM SPSS version 29 software. Both descriptive and quantitative analysis were performed showing the socio-demographic, clinical, and biochemical characteristics of participants. Distribution based on gender has been presented in the study. Data for continuous variables were expressed as mean and standard deviation (SD). In the case of categorical variables, data were presented in terms of count and percentage. All the presented data are based on the available values and percentages have been calculated from a total number of available values. Student t-test has been employed to determine the significance of differences between the means of soil and water parameters of hotspot and nonhotspot villages and a p-value of <0.05 was considered as significant.

Results

The demographic distribution of the whole population screened is shown in Table 1. The population's average age was 54±11.22 years, with male majority. The average BMI for the entire population is 23±9.62. According to the population's occupational status, the bulk of the population was in other categories (teachers, vendors, and businessmen), followed by farmers and laborers. The majority of participants had primary or higher primary education, followed by a degree, with very few being illiterate. The majority of the population has an average income level, while 1/4, or 25%, has a high-income level, while 14.9% of the population belongs to the low-income category. Around 13.5% of the population was addicted to tobacco products, and 5.59% of those consumed alcohol.

Table 1: Demographic characteristics of overall population

Parameters	Values
Overall population screened	2109
Age (mean ± SD)	54 ± 11.22
No. of males	1083
No. of females	1026
H/o hypertension	80
H/o diabetes	70
Body mass index (mean ± SD)	23 ± 9.62
Occupation	
Farmers	753
Labors	345
Others	1011
Level of education	
Illiterates	110
Primary	1163
Upper primary	708
Degree	128
Income	
High	539
Average	1254
Low	316
H/o tobacco use	285
Alcohol use	118

H/o: History of; SD: Standard deviation.

Out of the total population screened, 337 were identified as having CKD, among them 285 had CKDu while 52 patients had CKD from known etiologies. A greater prevalence of CKDu cases was observed in hotspot villages, in comparison to CKD cases as shown in Table 2. Lachida village in Attabira block reported the highest prevalence of CKDu. while the second highest prevalence was shown at M. Srigida in Bijepur block. The highest CKD cases were recorded at Kusanpuri village of Bhatli block. Interestingly, it was observed that some of the villages such as Lastala, Badipali, Mahulpali, Charpali, and Tala reported only CKDu cases and no CKD cases from known causes.

A large proportion of the population screened, 13.51% was found to be afflicted by CKDu, while 2.46% of the population had CKD from a known etiology. The majority of CKDu patients were young. Compared to females, males were more likely to be affected with CKD and CKDu. In CKD patients, hypertension and DM were more prevalent than in the general population. Patients with CKD and CKDu had higher BMIs than the general group.There was a preponderance of farmers in those affected with CKDu. The incidence of CKD and CKDu was higher in the illiterate and lower income groups than in the literate and higher/average income groups [Table 3].

A total of seven major pesticide residues were obtained when the soil and water samples were analyzed using LC–MS/MS. Organochlorine pesticides such as Endosulfan, Carbofuran, Paraquat as well as Cypermethrin were

Table 2: Distribution of CKD and CKDu in identified hotspot

Hotspot villages	CKD cases n(%)	CKDu cases n(%)
Arda	8 (15.3)	24 (8.4)
Manoharpali	2 (3.8)	19 (6.6)
Semelgudia	6 (11.5)	12 (4.2)
Mahulpali	0 (0)	20 (7.0)
Charpali	0 (0)	5 (1.7)
Salpali	3 (5.7)	19 (6.6)
M Srigida	1 (1.9)	28 (9.8)
Jamutbahal	5 (9.6)	17 (5.9)
Khairapali	6 (11.5)	9 (3.1)
Badipali	0 (0)	11 (3.8)
Lastala	0 (0)	26 (9.1)
Lachida	2 (3.8)	36 (12.6)
Budapali	5 (9.6)	14 (4.9)
Tala	0 (0)	4 (1.4)
Kusanpuri	11 (21.1)	19 (6.6)
Talpadar	3 (5.7)	22 (7.7)
Total	52	285

CKD: chronic kidney diseases; CKDu: chronic kidney diseases of unknown etiology.

observed to be many folds above the permissible limit in every hotspot village in both water and soil samples, whereas DDT was found to be marginally above the MRLs in some of the hotspot villages. Malathion and chlorpyriphos although detected in both water as well as soil samples in hotspot villages, their concentration was found to be within the permissible limits. Significant differences in the concentration of DDT, chlorpyrifos, endosulfan, malathion, and paraquat were observed in soil samples of hotspot and nonhotspot villages, whereas in water samples of both the areas, only chlorpyrifos and cypermethrin showed significant differences [Table 4].

Discussion

The present study identified 16 villages belonging to 5 different blocks having CKD/CKDu incidence above the national average of 8.02%,[5] and these were designated as hotspot villages. It was interesting to note that most of these identified CKD hotspot villages came under intensive agricultural zones with extensive use of pesticides. Unlike many other parts of the country, it was observed that a large number of people below 40 years of age were suffering from CKD. The average age group of CKD cases was 53±8.32, and that of CKDu was found to be 46 ±11.82 in Bargarh district. A study done in the Cuttack district of Odisha state, India, reported that the mean age of the cases to be 49 ± 10.62 years.[27] A similar study carried out in Karnataka state among a rural population showed that the mean age group of CKD cases is 52.73 ± 17.08 years.[26] It is well known that the chances of CKD increase with age because of associated chronic comorbid conditions such as hypertension, DM, and age-related loss of endogenous renal function.[28,29] More number of younger individuals were affected with CKDu in our study, suggesting the possible involvement of environmental factors contributing to CKD.

Table 3: Comparative representation of demographic characteristics between those with CKDu, those with CKD due to other causes, and healthy individuals

Paremater	CKD patients	CKDu patients	Normal population
Number of patients	52	285	1772
Age (mean+/-SD)	53 ± 8.32	46 ± 11.82	48 ± 3.44
No. of male	38	210	1098
No. of female	14	75	674
H/o hypertension	49	Nil	31
H/o diabetes	42	Nil	28
Body mass index (mean+/-SD)	26 ± 5.8	29 ± 3.11	21 ± 5.22
Occupation			
Farmers	28	133	592
Labors	7	66	272
Others	17	86	908
Level of education			
Illiterates	17	26	67
Primary	14	160	989
Upper primary	12	89	607
Degree	9	10	109
Income			
High	06	69	464
Average	24	97	1133
Low	22	119	175
H/o tobacco use	28	43	187
Alcohol use	34	26	58
Serum creatinine (mg/dl)	3.35 ± 0.03	3.89 ± 0.12	1.16 ± 0.21
Proteinuria (PCR)	1.6 ± 0.8	0.4 ± 0.1	0.5 ± 0.1

CKD: chronic kidney disease; CKDu: chronic kidney disease of unknown etiology; H/o: History of; SD: Standard deviation; PCR: protein creatinine ratio.

CKDu dominates in the present study in comparison to CKD in most of the hotspot villages. A higher prevalence of CKDu has been reported in many developing countries including India where the majority of CKDu patients were younger, poorer, and more likely to present with advanced stages of CKD.[30,31] Focal evidence from some parts of the country supports the fact that most of the patients diagnosed with CKDu are exposed to water resource contaminated with heavy metals, heat, and various drugs.[29,32,33] The strong association between the drinking water sourced from tubewell or borewell and CKD has been demonstrated across the globe.[34] Groundwater contamination may result from heavy metals leaching from different rocks or anthropogenic disposal to aquatic bodies. Contamination of groundwater with heavy metals is also reported to be associated with the induction of CKD among different populations.[35] A study in Sri Lanka reported a

Table 4: Assessment of nephrotoxic pesticide residues in soil and surface water of hotspot and nonhotspot regions

Pesticides	Soil (mg/kg) dry wt						Water (µg/L)					
	MRLs (mg/kg)	Hotspot region N = 48		Nonhotspot region N = 43		P value	MRLs (µg/L)	Hotspot region N = 48		Nonhotspot region N = 43		P value
		Mean	Range	Mean	Range			Mean	Range	Mean	Range	
DDT	0.05	0.043	BDL – 0.089	0.019	BDL - 0.027	0.46*	1	0.042	BDL – 0.09	0.003	BDL - 0.06	0.63
Chlorpyrifos	0.5	0.471	0.223 – 0.723	0.179	0.170 -0.211	0.27*	30	0.347	0.003 – 0.672	0.022	0.001 - 0.134	0.23*
Endosulfan	0.02	0.45	BDL – 0.96	0.011	BDL - 0.032	0.28*	0.4	0.395	0.007 – 0.79	0.009	BDL - 0.3	0.71
Malathion	0.4	0.467	BDL – 0. 93	0.322	0.004 – 0.78	0.42*	190	3.890	0.089 – 7.705	0.001	BDL - 0.05	0.65
Carbofuran	0.10	0.67	0.47 – 0.89	0.062	0.049 - 0.078	0.81	-	2.407	0.55 – 4.26	1.027	0.028 - 1.06	0.79
Paraquat	0.1	6.01	1.32-12.7	0.510	0.960 – 4.26	0.02**	-	0.4	0.02 – 0.78	0.001	BDL - 0.0038	0.64
Cypermethrin	2	1.567	0.029 – 3.143	0.027	0.021 -0.035	0.62	-	0.31	0.025 – 0.038	0.012	0.01 - 0.018	0.35*

MRL: maximum residue levels; DDT: Dichlorodiphenyltrichloroethane; BDL: below detectable limits; *- indicates $p < 0.05$; **-indicates $p < 0.05$.

higher incidence of CKDu due to heavy metal pollution of groundwater and aquifer leaching.[36] Although we have not assessed the heavy metal contents in groundwater in the hotspot villages in our study, their association with CKD incidence cannot be ruled out.

As our study sites are located in an area with intensive agriculture and widespread use of pesticides with known nephrotoxic effects, it is possible that agrochemicals may enter groundwater through aquifers from the earth's surface.[37] Although a direct correlation between the prevalence of CKDu and pesticide use cannot be established with the present data set, but the detection of nephrotoxic pesticides such as DDT, chlorpyrifos, endosulfan, malathion, paraquat, and cypermethrin in concentrations above the permissible limit in water and soil samples of hotspot villages in compression with nonhotspot villages indicates a possible association of intense pesticide use and increased prevalence of CKDu in this region. Similar to our findings, a number of studies have shown a higher prevalence of CKDu in the regions with intense pesticide use and in agricultural communities.[37–39] Studies carried out in the southern part of India mostly in the state of Andhra Pradesh[40] demonstrated a higher prevalence of CKDu among farming communities although a direct positive correlation has not yet been established in any of the studies in India. In a matched case–control study in the rural population of Shivamogga district of Karnataka, pesticides as well as heavy metals in blood and urine samples of CKD patients at the early stage showed higher heavy metal burden among affected populace indicating possible association with the progression of CKD.[41] Research shows gender differences as standard prognosticators for a decline in renal function, namely proteinuria among males and poor glycemic control among females.[28,42] High CKD cases among males in our study may be linked to their socio-behavioral and occupational practices, such as higher exposure to sunlight, longer working hours in the agricultural field, exposure to pesticides, and habitual consumption of locally made alcohol, which itself may be contaminated with toxic additives.[27] In our study area, 41% of the affected population were found practicing farming activities and that of 22% were laborers. The use of self-prescribed drugs such as painkillers and herbal supplements after exhausting physical activity was observed to be high, which could lead to varying expression of nonsteroidal anti-inflammatory drug-induced nephrotoxicity.[43] In India, DM and hypertension account for 40%–60% cases of CKD.[44] Singh *et al*. reported hypertension to be associated with low estimated GFR.[32] Screening of the population in different hotspot villages in the present study indicates that 2.4% of individuals suffering from CKD had a history of either DM or prolonged hypertension or both. More interestingly, a higher percentage (13.5%) of CKD in the younger population without having any history of either DM or hypertension indicated the role of environmental contaminants causing alteration of renal functions. A number of studies have suggested an association between pesticides and heavy metals and CKDu in humans.[45] In the present study, the presence of nephrotoxic pesticide residues in the soil and surface water of the identified hotspot regions provides indirect evidence of their involvement in the onset and progression of CKD in those areas. However, it is necessary to establish this association through the identification of entry pathways of these pesticide residues into the population. The greater prevalence of CKD is found in the farmer community, which may be due to direct exposure to pesticides and/or due to continuous heat exposure in crop fields. Reports indicate that the flow of pesticides occurs from soil to edible crops and reaches into the human body through food chain and biomagnification.[46] Nephrotoxic pesticides also reach humans directly by the consumption of contaminated water.[17] Understanding the detailed intrinsic properties of factors such as heat stress, ground water contamination, duration, and exposure of various antibiotics could help in unfolding the cause of higher CKD prevalence in this region.

Similar to that of Uddaman, Mesoamerica, and Sri Lankan nephropathy, water-borne agrochemicals and heavy metals, prolonged exposure to heat stress among farming communities and laborers possibly play a crucial role in causing CKDu. There is a need for a multipronged approach to address this CKDu epidemic through awareness, screening, and surveillance. Systematic research and special provisions for renal replacement therapy should be in place through increased government spending on health care.

Conclusion

This study reveals a concerning trend of elevated chronic kidney disease (CKD) and CKD of unknown etiology (CKDu) in sixteen hotspot villages within intensive agricultural zones, surpassing national averages. The presence of CKDu among younger individuals suggests potential environmental factors, possibly exposure to nephrotoxic pesticide residues. Nephrotoxic pesticides such chloropyrifos, endosulfan, paraquat, and cypermethrin were found to be signiificantly high in soil as well as water used in these hotspot villages. However, association between prevalence of CKD and exposure to pesticide residues has not been established with this limited data set. These findings underscore the critical need for targeted interventions, including heightened awareness, systematic screening, and improved healthcare access, to combat this public health issue.

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Conflicts of interest

There are no conflicts of interest.

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