

## Original Research Article

# A study on causes of chronic kidney disease in patients without diabetes mellitus and systemic hypertension in a tertiary care hospital

Praveen J.<sup>1\*</sup>, Tumbanatham A.<sup>1</sup>, Sivashankar M.<sup>2</sup>

<sup>1</sup>Department of General Medicine, <sup>2</sup>Department of Nephrology, Mahatma Gandhi Medical College and Research Institute, Puducherry, India

**Received:** 10 April 2022

**Revised:** 30 April 2022

**Accepted:** 05 May 2022

### \*Correspondence:

Dr. Praveen J.,

E-mail: [jpraveenanto@gmail.com](mailto:jpraveenanto@gmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

## ABSTRACT

**Background:** Chronic kidney disease is an increasing health problem worldwide. Thus apart from the well-established risk factors for CKD such as diabetes and systemic hypertension, the possibility that environmental, demographic, and various other risk factors an influence in developing chronic kidney disease has been assessed in several studies. Hence, the present study aimed to study the clinical and laboratory profile of chronic kidney disease in non-diabetic and non-hypertensive patients.

**Methods:** The study was enrolled 100 patients diagnosed with chronic kidney disease without diabetes and systemic hypertension in the department of general medicine and department of nephrology in a tertiary care hospital, Pondicherry for 1 year. The baseline data such as socioeconomic status, history of self-consumption of natural medicine and NSAIDs, their occupations, location of their living place, and routine laboratory parameters were collected and analysed.

**Results:** The socioeconomic status of the present study revealed that upper lower class was the predominant status and the majority of the patients were housewives and farmers. 38% of the patients were exposed to insecticides that were associated with CKD ( $p=0.0327$ ). 40% of the study population was victims of NSAID consumers ( $p=0.0236$ ). 42% was consumed natural medication on their own for their illness 46 without any consultation ( $p=0.0324$ ). The patients came from Cuddalore predominantly (22%).

**Conclusions:** Insecticide exposure, self-consumption of NSAIDs, and natural medicine are the main causes that progress to CKD in the present study.

**Keywords:** CKD, NSAIDs, Insecticide, Natural medicine, Risk factors

## INTRODUCTION

Chronic kidney disease (CKD) has the potential to be a significant contributor to negative health outcomes, and it is now recognized as an independent risk factor for cardiovascular disease events. Over the last two decades, there has been a significant increase in the global burden of chronic kidney disease (CKD).<sup>1</sup> Globally, the prevalence was predicted to be 147.6 million in 1990, and it has increased to 275.9 million in 2016, according to the

World Health Organization. Over the last two decades, the crude mortality rate has more than doubled, rising from around 0.59 million to 1.2 million people each year.<sup>2</sup> When compared to high-income developed countries, the prevalence of chronic kidney disease is disproportionately high in lower and middle-income economically developing countries (>15 percent higher).<sup>3</sup> Although the underlying cause of chronic kidney disease (CKD) differs from country to country, hypertension and diabetes are the most common causes worldwide.<sup>4</sup>

However, there has been a significant increase in the incidence and prevalence of chronic kidney disease (CKD) of unknown etiology (CKDu) over a wide range of geographical regions, despite the absence of any well-established risk factors.<sup>5-7</sup> Because it is widely found in low-income, tropical/subtropical countries, rural and middle-aged males, and comparable professions demanding physical labor, it is classified as a hazard. Researchers and physicians have become increasingly interested in CKDu in recent years.<sup>8</sup> CKD of unknown etiology (CKDu) is a term that has been used to characterize CKD that is not linked to any typical risk factor such as diabetes, high blood pressure, or HIV. It is becoming increasingly common to record cases of CKDu all over the world, and in many countries of Central and South America, as well as Eastern Europe and South Asia, it is being documented in epidemic proportions.<sup>9-11</sup> According to data from the Indian CKD Registry, CKDu is the second most prevalent underlying cause of CKD (16.0 percent), following diabetic nephropathy as the most common underlying cause (31.3 percent).<sup>12</sup> Different environmental and occupational exposures, including heat stress, dehydration, agricultural chemicals (pesticides, herbicides, fertilizers), heavy metals (cadmium, lead, arsenic) and infections are implicated in the development of CKDu as a multifactorial etiology. It is life-threatening because of the late detection and rapid advancement of the disease. Numerous studies have been conducted to ascertain the prevalence of CKD in non-diabetic and non-hypertensive patients in India. This study is taken up to highlight the clinical and laboratory profile of patients diagnosed with chronic kidney disease who are non-diabetic and non-hypertensive and to find out if there is any modifiable risk factor for this type of CKD in and around Pondicherry.

### ***Aim and objectives***

Aim and objective of current study were to estimate clinical and laboratory profile of chronic kidney disease in nondiabetic and non-hypertensive patients. The objectives of this study were to study the clinical and laboratory profile of chronic kidney disease in nondiabetic and non-hypertensive patients and to study the association of various factors in relation to chronic kidney disease in non-diabetic and non-hypertensive patients.

## **METHODS**

### ***Study design and population***

The study was a cross-sectional observational study. The study was conducted on both in-patients and out-patients diagnosed to have chronic kidney disease without diabetes mellitus and systemic hypertension in the department of general medicine and department of nephrology in Mahatma Gandhi medical college and research institute, Pondicherry between the period of one year from April 2020 to May 2021.

### ***Inclusion criteria***

All CKD as per KDIGO guideline 2012 and those aged above 18 years of age were included in the study.

### ***Exclusion criteria***

Patients with history of diabetes mellitus and systemic hypertension were excluded from the study.

### ***Sample size calculation***

The sample size is calculated based on the number of patients diagnosed to have chronic kidney disease without diabetes and systemic hypertension in a tertiary care hospital, which is approximately around 20%. As we couldn't get any study showing percentage of CKD in non-diabetic and non-hypertensive patients, the expected sample size for my study is taken as 100 (n).

### ***Data collection***

The patient demographic details, occupation history, history, personal history, reports of lab parameters such as hemoglobin, serum urea, creatinine, sodium, potassium, urine albumin, and glucose were collected. Also, the details of insecticide exposure, NSAIDs intake, and natural medication intake were collected from all the study patients.

### ***Statistical analysis***

The data was entered with an excel sheet. Data was exported to Medcalc version 19.0 for further processing. All categorical variables were expressed as percentages and the continuous variables were expressed as mean±standard deviation. The statistical significance of association among factors using the Chi-square test. All values were considered significant if the p value was <0.05. This research was strictly fulfilling the ethical guidelines as outlined in the declaration of Helsinki, participants signed a consent form, and were assured that their participation was completely voluntary and could be terminated at any time without compromising their medical care.

## **RESULTS**

The present study enrolled patients without diabetes mellitus and hypertension with the mean age of 55.6±16.40 years with the range of 16 to 88 years.

## **DISCUSSION**

There has been a lot of discussion, but there hasn't been any published study in India on particular environmental risk factors for CKD. Significant amounts of silica and other heavy metals in water, extended dehydration, heat stress, nonsteroidal anti-inflammatory medication use, traditional medicines, and high pesticide use have all

been proposed as theories.<sup>13,14</sup> Despite the fact that many of these theories have logical foundations and even some evidence from other parts of the world, epidemiological evidence is still lacking in order to construct a robust evidence base.

**Table 1: Demographic profile of the study participants.**

Variable	Frequency	%
<b>Gender</b>		
Male	56	56
Female	44	44
<b>Socioeconomic status</b>		
Upper lower	34	34
Lower	30	30
Lower middle	24	24
Upper middle	12	12
<b>Occupation</b>		
Housewife	31	31
Farmer	31	31
Coolie	13	13
Private employee	9	9
Others	8	8
Students	4	4
Retired	4	4

**Table 2: Risk factor among the study participants.**

Variable	Frequency	Percentage	P value
<b>Smoking</b>			
Yes	36	36	0.2970
No	64	64	
<b>Alcoholic</b>			
Yes	41	41	0.2532
No	59	59	
<b>Insecticide exposure</b>			
Yes	38	38	0.0327
No	62	62	
<b>Taken NSAID</b>			
Yes	40	40	0.0324
No	60	60	
<b>Consumption of natural medication</b>			
Yes	42	42	0.0236
No	58	58	

**Table 3: Baseline laboratory profile of the study participants.**

Variable	Mean±SD
Hemoglobin	8.85±1.83
Urea	124.83±77.92
Creatinine	5.35±3.66
Sodium	132.38±13.38
Potassium	4.66±0.94

**Table 4: Status of urine albumin levels.**

Urine albumin	Frequency	%
Trace	22	22
1+	24	24
2+	18	18
3+	11	11
Nil	25	25

**Table 5: Location of the study participants.**

Location	Frequency	%
Cuddalore	22	22
Panruti	12	12
Kurinjjipadi	12	12
Pondicherry	11	11
Viruthachalam	9	9
Chidambaram	5	5
Kallakurchi	4	4
Ariyalur	4	4
Chinnasalem	3	3
Villupuram	2	2
Lalgudi	1	1
Mayiladuthurai	1	1
Nellikupam	1	1
Thirunindravur	1	1
Srimushnam	1	1
Panathu	1	1
Pushpalam	1	1
Thindivanam	1	1
Sirkali	1	1
Thirunindravur	1	1
Nagapattinam	1	1
Vidayampallyagam	1	1

The most common theory is that drinking water has been contaminated. Several agencies and research groups have analysed the water, with an emphasis on heavy metals, but no consistent abnormalities have been discovered. Water samples obtained in the Uddanam area had a significant silica level, according to one study.<sup>14</sup> According to hydro chemicals data from another study, the groundwater in Uddanam is less mineralized than in other areas.<sup>15</sup> In the Andhra Pradesh district of Uchapally, Khandare et al discovered elevated amounts of strontium and silica in the drinking water.<sup>16</sup> None of these, on the other hand, has been reliably related to renal injury. High amounts of total dissolved solids in water samples from Uddanam have recently been discovered, which could imply high salinity as a result of seawater intrusion into freshwater aquifers and explain the high prevalence of hypertension and/or proteinuria.<sup>17</sup> The findings of the current study matched those of the previous study report. However, we did not evaluate the heavy metals present in the portable water sample drunk by the patients in this investigation.

In Uddanam, Tatapudi et al were unable to find any evidence of a link between pesticide use and CKDu.<sup>18</sup>

They relied on self-reporting, which is prone to recall bias, rather than biological markers (pesticide concentrations in blood or urine). In the urban population of Delhi (non-agricultural community) diagnosed with CKDu, Ghosh et al discovered a negative connection between organochlorine pesticides in the blood and the eGFR.<sup>19</sup> Few pesticides used in India and around the world have been related to CKD, and studies have been challenging to conduct due to the remote exposure compared to results and the multiple risk factors of CKD. Insecticide exposure could be a cause of CKDu, according to the findings of this investigation. This observation was by the previous study reports. In Taiwan and the United States, an ecological relationship between air pollution and CKD has been discovered.<sup>20,21</sup> India is home to 22 of the world's 30 most polluted cities.<sup>22</sup> Air pollution is caused by the burning of crops and plastic debris in both rural and urban regions. In rural Indian families, biomass-fueled cooking stoves are prevalent. In India, air pollution has yet to be considered as a contributor to CKD. Based on the findings of the current investigation, the same conclusion was reached.

Data from Taiwan in recent years have revealed the fascinating prospect of a role for previous *Leptospira* infection in the development of CKDu.<sup>23</sup> *Leptospirosis*, which was common in Tamil Nadu and Kerala until around 15 years ago, has witnessed a significant drop in incidence, making its significance in the development of CKD in India doubtful. Finally, the function of genetic variables has received little attention. Family history of kidney disease was found to be an independent predictor of CKD in the STOP-CKDu research. Prasad et al observed a substantial correlation of CKDu with single nucleotide polymorphisms associated to the NLRP4 and PRKN genes in a genome-wide association analysis involving 56 cases from Jharkhand categorised as having CKDu and 40 controls.<sup>24</sup> In the present study, we did not analyze any genetic factors and leptospiral infections in the patients. But we had analyzed NSAIDs and natural medicine consumption without any prescription. No other earlier comparable study is available to compare our study results. The mean hemoglobin level of the study participants in the present study was 8.85. The mean urea, creatinine level was 124.83±77.92 and 5.35±3.66. The mean sodium and potassium level was 132.38±13.38 and 4.66±0.94 respectively. Similarly in a study done by Fernando et al, it was shown that the median sodium and potassium was 142 and 4.5 respectively.<sup>25</sup> The mean hemoglobin was 8.6±15.3.

## CONCLUSION

In conclusion, CKD is a growing health problem in India, with increasing recognition that kidney disease often develops in individuals who do not have traditional risk factors like diabetes mellitus and hypertension. All patients were found to have anemia and azotaemia. The insecticide exposure, natural medication, and NSAIDs without consultation of medical practitioners are the risk

factors for CKD in this study. Also, the vulnerable population was housewives and farmers and the socioeconomic status of the victims have belonged to the upper-lower, and lower class. All the patients were found to have anemia and azotaemia.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Xie Y, Bowe B, Mokdad AH. Analysis of the global burden of disease study highlights the global, regional, and national trends of chronic kidney disease epidemiology from 1990 to 2016. *Kidney Int.* 2018;94:567-81.
2. Vos T, Abajobir AA, Abbafati C. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet.* 2017;390:1211-59.
3. Ene-Iordache B, Perico N, Bikbov B. Chronic kidney disease and cardiovascular risk in six regions of the world (ISN-KDDC): a cross-sectional study. *Lancet Glob Health.* 2016;4:e307-19.
4. Couser WG, Remuzzi G, Mendis S, Tonelli M. The contribution of chronic kidney disease to the global burden of major noncommunicable diseases. *Kidney Int.* 2011;80:1258-70.
5. Gifford FJ, Gifford RM, Eddleston M, Shaun N. Endemic nephropathy around the world. *Kidney Int Rep.* 2017;2:282-92.
6. Jayasumana C, Paranagama P, Agampodi S, Wijewardane C, Gunatilake S, Siribaddana S. Drinking well water and occupational exposure to herbicides is associated with chronic kidney disease, in Padavi-Sripura, Sri Lanka. *Environ Health.* 2015;14:6.
7. Redmon JH, Elledge MF, Womack DS, et al.: Additional perspectives on chronic kidney disease of unknown etiology (CKDu) in Sri Lanka--lessons learned from the WHO CKDu population prevalence study. *BMC Nephrol.* 2014;15:125.
8. Correa-Rotter R, Wesseling C, Johnson RJ. CKD of unknown origin in Central America: the case for a Mesoamerican nephropathy. *Am J Kidney Dis.* 2014;63:506-20
9. Orantes CM, Herrera R, Almaguer M, Brizuela EG, Hernández CE, Bayarre H, et al. Chronic ~ kidney disease and associated risk factors in the Bajo Lempa region of El Salvador: Nefrolempa study, 2009. *MEDICC Rev.* 2011;13:14-22.
10. Martin-Cleary C, Ortiz A. CKD hotspots around the world: Where, why and what the lessons are. A CKJ review series. *Clin Kidney J.* 2014;7:519-23.
11. Correa-Rotter R, Wesseling C, Johnson RJ. CKD of unknown origin in Central America: The case for a

- Mesoamerican nephropathy. *Am J Kidney Dis.* 2014;63:506-20.
12. Rajapurkar MM, John GT, Kirpalani AL. What do we know about chronic kidney disease in India: first report of the Indian CKD registry. *BMC Nephrol.* 2012;13:10.
  13. John O, Gummudi B, Jha A, Gopalakrishnan N, Kalra OP, Kaur P, 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.
  14. Ghahramani N. Silica nephropathy. *Int J Occup Environ Med.* 2010;1:108-15.
  15. Reddy D, Gunasekar A. Chronic kidney disease in two coastal districts of Andhra Pradesh, India: role of drinking water. *Environ Geochem Health.* 2013;35:439-54.
  16. Khandare AL, Reddy YS, Balakrishna N. Role of drinking water with high silica and strontium in chronic kidney disease: an exploratory community-based study in an Indian Village. *Indian J Commu Health.* 2015;27:95-102.
  17. Lal K, Sehgal M, Gupta V. Assessment of groundwater quality of CKDu affected uddanam region in Srikakulam district and across Andhra Pradesh, India. *Groundwater Sustain Develop.* 2020;11:100432.
  18. Tatapudi RR, Rentala S, Gullipalli P. High prevalence of CKD of unknown etiology in Uddanam, India. *Kidney Int Rep.* 2018;4:380-9.
  19. Ghosh R, Siddarth M, Singh N. Organochlorine pesticide level in patients with chronic kidney disease of unknown etiology and its association with renal function. *Environ Health Prevent Med.* 2017;22:1-8.
  20. Lin S-Y, Ju S-W, Lin CL. Air pollutants and subsequent risk of chronic kidney disease and end-stage renal disease: a population-based cohort study. *Environmen Pollut.* 2020;261:114.
  21. Bowe B, Xie Y, Li T. Particulate matter air pollution and the risk of incident CKD and progression to ESRD. *J Am Soc Nephrol.* 2018;29:218-30.
  22. The World's 30 Most Polluted Cities Are In India: Report India 2021. Available at: <https://www.ndtv.com/indianews/22-of-the-worlds-30-most-polluted-cities-are-in-india-delhi-most-polluted-capital-city-report-2392028>. Accessed on 20 November 2021.
  23. Yang CW. Leptospirosis renal disease: emerging culprit of chronic kidney disease unknown etiology. *Nephron.* 2018;138:129-36.
  24. Prasad N, Prakash S, Kahn Aw, Bhadauria D, Gupta A. SUN-01 genome wide analysis study to evaluate potential genetic risks and immunological pathways associated with chronic kidney disease of unknown etiology. *Kidney Int Rep.* 2019;4(7):S242.
  25. Fernando BN, Sudeshika TS, Hettiarachchi TW, Badurdeen Z, Abeysekara TD, Abeyundara HT, et al. Evaluation of biochemical profile of Chronic Kidney Disease of uncertain etiology in Sri Lanka. *Plos One.* 2020;15(5):e0232522.

**Cite this article as:** Praveen J, Tumbanatham A, Sivashankar M. A study on causes of chronic kidney disease in patients without diabetes mellitus and systemic hypertension in a tertiary care hospital. *Int J Adv Med* 2022;9:694-8.