

## Original Research Article

# A study of chronic kidney disease patients with no known risk factors coming to tertiary care hospital

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**Received:** 02 March 2017

**Accepted:** 31 March 2017

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### ABSTRACT

**Background:** Chronic kidney disease (CKD) has become a major cause of morbidity and, in some parts of the world CKD incidence has increased regardless of hypertension, diabetes mellitus or metabolic syndrome. This study was done to identify the unknown factors which can be contributing to the increased incidence of CKD.

**Methods:** It was a case control study. There were 61 cases and 50 controls. A detailed history regarding residence, occupation, addiction, drug intake, family history, diet and environmental factors was taken. The data was analysed to identify a common factor amongst the CKD patients who did not have history of any known risk factors of CKD.

**Results:** Age of onset of CKD in 48% of cases was <40 years. Much higher percentage of cases gave family history of CKD (10%), history of consumption of NSAIDs (20%) and smoking for >5 years (30%) as compared to controls. Much more cases as compared to controls gave history of mixed diet (46% vs 26%). Much higher proportion of cases had history of heat exposure, excessive heating and sugarcane exposure (72%, 70% and 48% respectively) as compared to controls.

**Conclusions:** This study supports the association of sugarcane exposure, heat exposure and excessive sweating with CKD and reports a changing trend of renal involvement starting at an earlier age. It highlights need of study with sufficient sample size and greater emphasis on family history, smoking, extent of heat exposure and sugarcane exposure to help identifying area of further research and guide policy making.

**Keywords:** Case control study, Chronic kidney disease, Heat exposure, Sugarcane exposure

### INTRODUCTION

Chronic kidney disease (CKD) has become a major cause of morbidity and mortality throughout the world owing to the increasing incidence of obesity and diabetes. In 2010, CKD soared to 18th place from 27<sup>th</sup> in 1990 among global causes of mortality.<sup>1</sup> In the last two decades it has recorded the third largest increase in mortality (by 82%) after HIV/AIDS and diabetes.<sup>2</sup>

Hypertension and diabetic nephropathy are the two most common diseases which lead to end-stage renal disease apart from obesity and metabolic syndrome which also frequently lead to early involvement of kidneys, even

before diabetes and high blood pressure become apparent. However, in some parts of the world CKD incidence has increased despite absence or very low incidence of hypertension, diabetes mellitus or metabolic syndrome. Some studies have even reported absence of diabetes or hypertension in almost 40% of those identified with CKD in screening programs.<sup>3,4</sup>

These patients have been reported to be mostly young, therefore the health cost and quality of life are affected to a great extent. In our setup also we observed many young patients presenting with CKD without any history of diabetes or hypertension or any other known cause. Hence we carried out this study to identify the common

factor amongst these patients to which the cause of CKD can be attributed, to help in identifying the area of further research and guiding policies to contain any further surge.

## METHODS

It was a case control study carried out in Medicine department of a tertiary care hospital in Gujarat which is present on west coast of India.

The study started after approval from the institutional ethics committee. All patients with CKD (already diagnosed or diagnosed during admission) coming to OPD or IPD and who gave written informed cases as participants were enrolled as cases. CKD was defined as >3 months' presence of proteinuria, elevated levels of serum creatinine (>1.2 mg/dL) and confirmed abdominal ultrasound scan reports. Age and sex matched non-CKD subjects were recruited as controls subsequent to clinical and biochemical examinations.

The subjects having normal levels for the tested parameters and who complied with all the exclusion criteria of the CKD patients were selected as controls. Subjects of both groups were made aware of the research study and their written informed consent was obtained prior to their participation. A detailed history regarding

residence, occupation, addiction, drug intake, family history, diet and environmental factors was taken based on a standardized proforma. The data so collected was assessed to describe any dietary, occupational or environmental differences between the CKD and non CKD groups and identify the factors which had an association with CKD.

## RESULTS

Total 71 patients were enrolled. After exclusion for known risk factors, 61 were included in the study as cases. 50 age and sex matched healthy controls were selected for comparison as controls. The two groups were similar in terms of basic parameters (Table 1).

**Table 1: Basic characteristics of cases and controls.**

	Cases (n=61)	Controls (n=50)
Age	43.1±15.52 years	44.54±16.11 years
BMI	25.38±2.17 kg/m <sup>2</sup>	25.72±2.15 kg/m <sup>2</sup>
Males	46 (75.4%)	38 (76%)
Females	15 (24.59%)	15 (30%)
Hypertension	20 (32.78%)	15 (30%)
Diabetes mellitus	7 (11.47%)	5 (10%)

**Table 2: Distribution of salient features of history among cases and controls.**

	Cases (n=61)	Controls (n=50)
Family history of CKD	14 (22.95%)	1(2%)
History of tobacco chewing	27 (44.26%)	9 (18%)
NSAIDS	12 (19.67%)	5 (10%)
>5 years of alcohol	19 (31.14%)	9 (18%)
>5 years of smoking	19 (31.14%)	9 (18%)
Diet: vegetarian mixed	27 (54%)	37 (74%)
	23 (46%)	13 (26%)

36 (59%) of cases were <40 years of age as compared to 22 (44%) controls. On taking history much higher percentage of cases gave family history of CKD, tobacco chewing, consumption of NSAIDs, alcohol ingestion and smoking for >5 years as compared to controls.

Many more cases as compared to controls gave history of mixed diet (46% vs 26%) (Table 2).

History of environmental exposure revealed much higher proportion of heat exposure, excessive sweating and pesticide exposure amongst cases as compared to controls.

All other professions were equally distributed between the two groups (Table 3).

**Table 3: Distribution of occupation and exposure among cases and controls.**

	Cases (n=61)	Controls (n=50)
Heat exposure	43 (70.49%)	35 (70 %)
Excessive sweating	35 (70%)	9 (18%)
Pesticide	21 (34.42%)	15 (30%)
Chemical fumes	13 (21.31%)	12 (24%)
Vehicles	5 (8.19%)	6 (12%)
Dust/Cement	2 (3.27%)	1 (2%)
Occupation		
Farmer	29 (47.54%)	22(44%)
Driver	7 (11.47%)	2 (4%)
Industry worker	7 (11.47%)	2 (4%)
Others	18 (29.50%)	24 (48%)

On assessing association between various variables and CKD, a significant association of CKD was found with excessive sweating and heat exposure. Other than these, consumption of NSAIDs, recurrent UTI, positive family

history, history of ayurvedic treatment and exposure to pesticides were also found to be positively associated with CKD (Table 4).

**Table 4: Association of CKD with various components of history and exposure.**

	Case (n=61)	Controls (n=50)	Odds ratio	P- value
Age <40	36	22	1.83 (90.86 -3.90)	0.13
Farmer	29	22	1.15 (0.54 -2.44)	0.84
Long heat exposure	43	35	1.02 (0.45 -2.31)	0.9
NSAID	12	5	4.5 (1.41 -14)	0.012
Chemical fumes	13	12	1.21 (0.48- 3.01)	0.81
Tobacco chewing	27	9	3.51 (1.45 -8.46)	0.0045
Recurrent UTI	13	3	3.02 (1.84 - 7.76)	0.002
Family history	14	1	3.19 (1.25-5.86)	<<0.05
Ayurvedic treatment	14	3	2.05 (1.45 - 3.24)	0.009
Smoking	19	9	2.01 (0.81 -4.95)	0.187
Alcoholic	19	9	2.01 (0.81-4.95)	0.187
Pesticide	21	15	1.959 (1.14-3.87)	0.0008

## DISCUSSION

In our study a significant association of CKD was found with excessive sweating, heat exposure, consumption of NSAIDs, recurrent UTI, positive family history, history of ayurvedic treatment and exposure to pesticides. Remarkably, the history of sugarcane exposure was positive in 48% of cases while none of the controls gave such history. These observations were in accord with the results of various previous studies. Since the last two decades, there is an upsurge of studies reporting an entity called CKDu (CKD of unknown etiology) referring to those CKD cases in which no attributing factor to CKD could be identified. Studies from Central America have reported a new kidney disease Mesoamerican nephropathy which primarily affects agricultural communities especially in the sugarcane fields.<sup>1,5,6</sup> It was reported to present with mild proteinuria and asymptomatic progressive kidney failure. Kidney biopsies showed chronic tubulointerstitial disease with secondary glomerulosclerosis and some signs of glomerular ischemia. The authors suggested recurrent dehydration related to manual labor under very hot conditions in agricultural fields, possibly exacerbated by NSAIDs or other toxins as a likely cause.<sup>6</sup>

Studies from Sri Lanka and India have also reported outbreaks of CKD occurring among workers in the rice paddies. They reported that CKDu (CKD of unknown etiology) had a point prevalence ranging from 2–16% among those aged >18 years.<sup>7-9</sup> and that biopsy primarily showed tubulointerstitial involvement, secondary glomerulosclerosis and glomerular ischemia.<sup>1</sup> Some other case control and cross sectional studies suggested chronic exposure of people in the endemic area to low levels of

cadmium through the food chain and also to pesticides<sup>7</sup> or contamination of water, food or both by heavy metals, fertilizers and pesticides as the probable cause of CKDu.<sup>10</sup> Epidemiological data from clusters of cases of CKD from Taiwan and China have showed an association between use of herbs containing aristolochic acid and CKD.<sup>11,12</sup> Similarly, Balkan-endemic nephropathy, which affects people living along the tributaries of the Danube river in Europe, is now considered to be a form of aristolochic acid-related kidney disease.<sup>13</sup>

In two studies in India partially funded by the ISN Research and Prevention Committee, no excess of heavy metals was found in the water in the Srikakulam district (MS Ravishankar, Seven hills Hospital, Mumbai, India, personal communication), while contamination of ground water used for drinking purposes with trace elements such as silica was suspected of causing CKD described in rural villages in the state of Andhra Pradesh (G. Taduri, Nizams Institute of Medical Sciences, Hyderabad, India, personal communication).

In the latter case, a program for changing drinking water source was adopted by the communities and strict monitoring of the population for CKD was established. There have been many previous studies which reported that prevalence of CKD varied strongly with age. Four studies were conducted among elderly persons ( $\geq 64$  years) and showed a markedly high prevalence.<sup>14,17,18</sup> Several studies conducted in middle and old-aged persons ( $\geq 30$  years old) reported prevalence of CKD varying from 1.5% to 43.3% in different populations (median: 7.2%). The highest prevalence was reported from a cohort study among persons aged 45 years or older in USA (43.3%).<sup>19</sup> However, we observed that in >48% cases, the age of

onset of CKD was <40 years. This is contrary to the belief that eGFR declines in parallel with age.<sup>14</sup> Although the sample size was small, the study addressed an important issue of identifying factors which might lead to CKD in absence of known risk factors with a reasonable study design. The cases and controls were carefully selected so as to avoid any selection bias.

This study apart from supporting the previous reports of association of CKD with sugarcane exposure, dehydration and excessive sweating, identified few other factors like family history, recurrent UTI and pesticide exposure which might have an association with CKD.

## CONCLUSION

Excessive sweating, long exposure to heat and sugarcane, recurrent UTI, positive family history and exposure to pesticides may be the factors responsible for onset of CKD in cases without any obvious underlying cause. In view of the morbidity and mortality associated with the rapidly increasing population of CKD, this study highlights need of a study to assess correlation of these factors with CKD.

*Funding: No funding sources*

*Conflict of interest: None declared*

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

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**Cite this article as:** Muley A, Rathod M, Shah K, Patel N, Patel A, Bhuta P. A study of chronic kidney disease patients with no known risk factors coming to tertiary care hospital. *Int J Res Med Sci* 2017;5:2030-3.