



## CASE CONTROL STUDY TO IDENTIFY THE RISK FACTORS OF CHRONIC KIDNEY DISEASE

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### ABSTRACT

Chronic Kidney Disease (CKD) is a global issue and its risk factors differ between races and countries. The increase in incidence of CKD in the last decade attributes to the lifestyle changes which need to be identified. It is worth understanding the risk factors in India where there is diversity in the income, food, cultural traditions and lifestyle habits. This "case control study to assess the risk factors of chronic kidney disease among adults" was conducted among 200 subjects with the objectives to identify the risk factors of chronic kidney disease and to estimate the exposure to risk factors among patients with and without chronic kidney disease using retrospective survey design. The data were collected using a structured questionnaire and analysed using Odd's ratio (OR). The findings show that age (OR-2.6675, CI-95%, 1.443-4.957) and family history of CKD (OR-4.846, CI-95%, 1.020-23.0228) were the non-modifiable risk factors. Co-morbidities like hypertension (OR-18.971, CI-95%, 9.235-38.969), diabetes mellitus (OR-3.618, CI-95%, 2.017-6.490), coronary artery disease (OR-11.821, CI-95%, 4-34.933), urinary tract infections (OR-5.664, CI-95%, 2.460-13.043) and use of analgesics (OR-6, CI-95%, 2.186-16.467) were major modifiable risk factors. Modifiable risk factors play an important role in the development of CKD. So screening the patients at risk for CKD should be emphasized and treating the modifiable risk factors at an early stage will help to reduce the incidence and or progression of the disease. Prevention and control should also focus on the life style habits.

**KEYWORDS:** Chronic kidney disease (CKD), case-control study, risk factors, non-modifiable risk factors, co-morbidities, structured questionnaire.



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## INTRODUCTION

Chronic kidney disease (CKD) is a life threatening condition, which involves progressive, irreversible loss of kidney function. It is a progressive disease that arise from both non-communicable diseases and infectious diseases. The use of herbal nephrotoxic medications, such as those containing aristolochic acid, also contributes to CKD (Odds ratio = 2.19). Studies suggest that CKD may be a risk multiplier for infectious disease-associated mortality primarily in developing countries, which face comparatively higher infectious disease burdens.<sup>1</sup> Common diseases which lead to chronic kidney disease are malignant hypertension, infections, diabetes mellitus, focal segmental glomerulosclerosis; genetic causes which include polycystic kidney disease, a number of inborn errors of metabolism, and autoimmune conditions such as systemic lupus erythematosus. Early diagnosis and treatment of the underlying causes and institution of secondary preventive measures are imperative in patients with kidney disease to limit the worsening of renal function. Therefore, identification of risk factors will help to reduce the damage of kidney. The medical care of patients with kidney disease should focus on halting the progression of chronic kidney disease, treating the pathologic manifestations of chronic kidney disease, timely planning for long-term renal replacement therapy, including dialysis and transplantation.<sup>2</sup> A case control study will help to determine whether any association exists between the disease and the risk factors in the present population and also to compare the risk factors with healthy population. Evidence suggesting association of specific factors with CKD will help to identify those individuals who are likely to develop CKD. Moreover, it is also important to identify factors that increase the risk of CKD, even in individuals with normal GFR.

## MATERIALS AND METHODS

Quantitative approach using case control retrospective study design was adopted for the present study and was conducted in the Nephrology units and Comprehensive

Health Check up Centre of a selected referral hospital at Kochi, Kerala. Subjects for the study were divided into cases and control based on sample selection criteria. Hundred subjects each in case and control were selected.

### Inclusion criteria

#### Cases

The patients who were diagnosed with CKD between 30-70 years, admitted in selected wards or attending Nephrology OPD and dialysis unit with serum creatinine level >1.36 mg/dl and eGFR<30 mg/dl/1.73m<sup>2</sup> by using Cockcroft-Gault formula.

#### Controls

The patients who were not diagnosed with chronic kidney disease between 30-70 years attending comprehensive health check up centre, of the same hospital, with serum creatinine value <1.36mg/dl and eGFR>30 mg/dl/1.73 m<sup>2</sup> by using Cockcroft-Gault formula.

### Exclusion criteria

Patient who are critically ill, those undergone renal transplantation and who have cognitive impairment.

### Tools and procedure of data collection

Self-developed structured questionnaire was used to assess risk factors of chronic kidney disease which included socio-demographic data such as age, gender, marital status, education, occupation, monthly income and area of residence; clinical parameters, biophysical parameter and biochemical parameters and, personal habits like smoking, alcohol, type of diet, physical activity, consumption of medications. The presence of comorbidities like hypertension, diabetes mellitus, dyslipidemia, heart attack, stroke, recurrent urinary tract infections, history of renal stones, other renal diseases and family history of renal disease were assessed using a checklist.

### Ethical Consideration

The study was conducted after the approval from the Institutional Ethical Committee.

## RESULTS

**Table 1**  
**Exposure rate of CKD calculated using Odds Ratio (OR) n =200**

Sl. No	Risk factors	Control f	Cases f	Odd's Ratio	CI-95% lower/upper	p value
<b>A Non-Modifiable</b>						
1.	Age (in years)					
	30 - 45	43	22	2.675	1.443/4.957	0.002
	46 - 70	57	78			
2.	Family History of CKD					
	No	98	91	4.846	1.020/23.0228	0.47
	Yes	2	9			
<b>B Modifiable</b>						
1.	Hypertension					
	No	77	15	18.971	9.235/38.969	<0.001
	Yes	23	85			
2.	Diabetes Mellitus					
	No	68	37	3.618	2.017/6.490	<0.001
	Yes	32	63			

3.	Coronary Artery Disease					
	No	97	67	11.821	4/34.933	<0.001
	Yes	3	33			
4.	Urinary Tract Infection					
	No	92	67	5.664	2.460/13.043	<0.001
	Yes	8	33			
5.	History of renal stones					
	No	94	80	3.917	1.500/10.227	0.005
	Yes	6	20			
6.	Smoking					
	No	83	73	1.86	.912/3.577	0.90
	Yes	17	27			
7	Use of analgesics					
	No	95	76	6.000	2.18/16.46	0.001
	Yes	5	24			
8	Herbal medications					
	No	99	95	5.211	.522/7.82	0.212
	Yes	1	5			
9	Ayurvedic medicines					
	No	94	85	2.765	1.026/7.449	0.044
	Yes	6	15			
10	Obesity (↑BMI)					
	No	61	33	3.033	1.69/5.42	<0.001
	Yes	39	64			

*f* = frequency, *CI* = Confidence Interval, *L/U* = Lower/ Upper, *OR* = Odd's Ratio

Exposure risk calculated using Odd's Ratio (Table 5) indicate that advanced age (OR-2.675, 95% CI: L=1.443,U=4.957) and family history of chronic kidney disease (OR-4.846, 95% CI: L=1.020,U=23.0228) are the non-modifiable risk factors of chronic kidney disease among the selected subjects. The risk for CKD among hypertensive patients are 18.971 times frequent than normotensives and 3.618 times frequent in diabetics than non-diabetics. Other risk factor of CKD include coronary artery disease (OR-11.821, 95% CI, 4-34.93), UTI (OR-5.664, 95% CI, 2.46 -13.043), history of renal stones (OR-3.917, 95% CI, 1.500-10.227), smoking (OR-1.806, 95% CI, 0.912-3.577), consumption of junk food (OR-1.76,95% CI, 1.007-3.104) **and** obesity (OR-3.033, 95% CI, 1.696-5.425). The use of analgesics (OR-6, 95% CI, 2.186-16.467), use of ayurvedic medication (OR-2.765,95% CI, 1.026-7.444) and herbal medication (OR-5.211, 95% CI, .598-45.426) are other risk factors of CKD which are prevalent evidently in the case group.

## DISCUSSION

The present study findings show that age and family history of chronic disease are the major non-modifiable risk factor for CKD. The number of patient with CKD was found to increase as age advance ie.11%, 17%, 27% and 45% respectively among 30-39 years, 40-49 years, 50-59 years and 60-70 years of age group. So advancing age was a risk factor among the study population. Major non-modifiable risk factors of CKD among the total study subjects were age group of 46-70 years ie. 135 (67.5%). The comorbidities like hypertension and diabetes mellitus contributed as significant risk factor of chronic kidney disease among the cases. Consumption of junk food was a risk factor which is found in 62 of the cases. In the control group, 23 were hypertensive, 32 were known diabetics and consumption of junk food were found more prevalently in 48 subjects. Thus prevalence of risk factors in case group was evidently higher than that of the controls.

Other risk factors like family history of CKD (9 cases vs 2 control), history of smoking (27 cases vs 18 control), use of analgesics (24 cases vs 5 control), CAD (33 cases vs 4 control), history of renal stones (20 cases vs 6 control), UTI (33 cases vs 8 control), obesity (64 cases vs 39 controls) were higher among the cases than in control. In the present study there were 7 cases with stroke whereas none in the control group had history of cerebrovascular accident. The findings of the present study is supported by Oluyombo R, Ayodele OE, Akinwusi PO, Okunola OO, Akinsola A, Arogundade FA, Sanusi A, Onayade A<sup>3</sup> in 2013 to identify prevalence of CKD and its associated risk factors in Nigerian community among 468 residents aged >18 years. Smoking habit, habitual analgesic intake, alcohol and herbal concoction use was 7%, 20%, 19% and 75% respectively. The prevalence of hypertension was 30%, diabetes mellitus 3.7%, obesity by waist circumference 14.6% and hematuria 3.1%. The overall prevalence of CKD was 18.8%, with CKD stages 1, 2, 3 and 4 accounting for 2.4%, 4.1%, 11.8% and 0.5% respectively. Age (p=0.00; OR 1.09), female gender (p=0.006; OR 4.87), systolic blood pressure p<0.001; OR 1.04) and diabetes (p=0.0033; OR 15.76) were predictive of CKD. The prevalence of CKD and its risk factors like smoking, alcohol consumption and herbal medication **were** high in this rural community of South Western Nigeria. Freedman BI, Volkova NV, Satko SG, Krisher J, Jurkovitz C, Soucie JM, McClellan WM<sup>4</sup> conducted a population-based screening on family history of end-stage renal disease among patients in USA (2005) reported family history of ESRD among 22.8% of 55,929 subjects studied. The study concluded that incidence of CKD among the relatives of patients with CKD are rising. Thus findings of this study are consistent with the study findings of the present study. The major risk factors identified to cause CKD among the study subjects include the non-modifiable factors such as age and family history of CKD and the modifiable factors like hypertension, diabetes mellitus, coronary artery diseases, history of renal stones, urinary

tract infection, use of analgesics and ayurvedic medications and consumption of junk food. Najafi I, Attari F, Islami F, Shakeri R, Malekzadeh F, Salahi R et al<sup>5</sup> conducted a study to identify the renal function and risk factors of moderate to severe chronic kidney disease among 3,591 participants from general population, Northeast of Iran in 2010. The results of the study revealed that 35% of participants were overweight (BMI 25–29.9 kg/m<sup>2</sup>) and 24.5% were obese (BMI 30 kg/m<sup>2</sup>). Prevalence of CKD stages 3 to 5 i.e., GFR, 60 mL/min/1.73 m<sup>2</sup>, was 4.6%. The risk of CKD stages 3-5 associated with every year increase in age was 1.13 (1.11–1.15). Obesity (OR = 1.78; 95% CI, 1.04–3.05) and self-reported diabetes (OR = 1.70; 95% CI, 1.00–2.86), hypertension (OR = 3.16; 95% CI, 2.02–4.95), ischemic heart disease (OR = 2.73; 95% CI, 1.55–4.81), and myocardial infarction (OR = 2.69; 95% CI, 1.14–6.32) were associated with increased risk of CKD—S 3-5 is adjusted for age and sex. The study concluded that advanced age, obesity, diabetes mellitus, and coronary artery disease as the risk factors associated with CKD. This study is consistent with the present study findings in which hypertension (OR-18.971, CI 95%, 9.235-38.969), coronary artery disease (OR-11.821, CI 95%, 4-34.933), diabetes mellitus (OR-3.618, CI 95%, 2.017-6.490), obesity (OR-3.033, CI 95%, 1.69-5.42) were found to be the co-morbid conditions that contributed as risk factors. In the present study, personal habits like smoking (OR-1.806, 95% CI=0.912-3.577), alcoholism (OR-0.782, 95% CI=0.422-1.448) and hyperlipidemia (OR-1.63, 95% CI=0.929-2.86) were identified as the risk factors for CKD. Yacoub R, Habib H, Lahdo A, Ali RA, Varjabedian L, Atalla G, et al<sup>6</sup> (2010) conducted a case control study on association between smoking and chronic kidney disease. Smoking data was analyzed in patients with CKD throughout 2005-2009. One hundred and ninety-eight patients who had recently been diagnosed with stage-3 CKD or higher according to the National Kidney Foundation (NKF) 2002 classification were studied. The control group was randomly selected and then matched with the case subjects using a computerized randomization technique. Smoking significantly increased the risk of CKD (OR = 1.6, p = 0.009, 95% CI, 1.12-2.29). Smoking increased the risk of CKD for those classified as hypertensive nephropathy (OR = 2.85, p = 0.01, 95% CI, 1.27-6.39) and diabetic nephropathy (2.24, p = 0.005, 95% CI, 1.27-3.96). No statistically significant difference in risk was found for glomerulonephritis patients or any other causes but the risk to develop CKD among smokers were evident. The present study also support smoking as a risk factor. However, risk associated with glomerulonephritis is not assessed independently. Sera N, Hida, A, Imaizumi M, Nakashima E, Akahoshi M<sup>7</sup> conducted a study to associate CKD with cardiovascular disease risk factors in atomic bomb survivors of Japan. Among 1,040 atomic bomb survivors who were examined in 2004–2007, hypertension (OR 1.57; 95% CI, 1.12– 2.20, p ¼ 0.009); DM (OR, 1.79; 95% CI, 1.23–2.61, p ¼ 0.002); hyperlipidemia (OR, 1.55; 95% CI, 1.12–2.14, p ¼

0.008); and metabolic syndrome (OR, 1.86; 95% CI, 1.32–2.63, p 0.001) were associated with CKD (moderate/severe renal dysfunction), and hyperlipidemia and metabolic syndrome were also associated with mild renal dysfunction. This study is consistent with the present study findings. However, the radiation of atomic explosion can also contribute to the development of CKD in that population. White SL, Kevan R. Polkinghorne, Cass A, Shaw JE, Robert C et al<sup>8</sup> (2005) conducted a study on alcohol consumption and 5-year onset of CKD among 6,259 adults without a history of alcohol dependence from Australian population-representative study. The outcomes were as follows: (i) 5-year decline in estimated glomerular filtration rate (eGFR) ≥10%, with baseline eGFR ≥60 and final eGFR <60 mL/min/1.73 m<sup>2</sup>, and (ii) 5-year doubling of albumin to creatinine ratio (ACR) with final ACR ≥2.5 (males)/≥3.5 (females) mg/mmol, in the absence of albuminuria at baseline. Self-identification as a moderate or heavy, versus light, drinker was associated with elevated risk of albuminuria in males and females <65 years of age (OR, 95% CI: males 1.87, 0.99–3.52; females 2.38, 1.37–4.14). Odds of eGFR <60 mL/min/1.73 m<sup>2</sup> were 0.34 (95% CI 0.22–0.59) and 0.68 (95% CI 0.36–1.27) in males and females, respectively, who were moderate–heavy drinkers. The researcher concluded that moderate-heavy alcohol consumption may be an important modifiable risk factor for albuminuria in the general population. These studies support the present findings where alcohol consumption was found to be a major risk factor. The study has limitations such as lack of randomization. So, the generalization is limited to the study participants.

## CONCLUSION

Advancing age, family history of CKD, smoking, junk food, lack of exercise, intake of ayurvedic medications, use of analgesics and comorbidities like hypertension, diabetes mellitus, coronary artery disease, urinary tract infection, kidney stones were found to be the risk factors of CKD among the cases. Majority of these factors being modifiable, there is a need for making the public aware about the importance of reducing the exposure to these factors. Nurses, being the frontiers in the health care scenario, need to take initiative in conducting awareness programs thereby keeping the goal of protecting kidney as a precious organ. So, the nurses in the clinical as well as community settings play a vital role in assessment of the kidney function, creating awareness among the public regarding the importance of protecting the kidney, identification and elimination of risk factors to protect from diseases affecting the kidneys and possible complications.

## CONFLICT OF INTEREST

Conflict of Interest declared none.

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