Determinants of Chronic Kidney Disease among Young Adults attending a Tertiary Care Hospital in Madurai- A Case-Control Study.

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Abstract:

Introduction: As with other non-communicable diseases, chronic kidney disease (CKD) also is in a way at the top among the younger population. Apart from diabetes, hypertension, old age, family history of CKD other risk factors like smoking, alcohol, pesticide exposure, heavy metals also made them vulnerable to CKD. The focus on CKD in younger age groups is often overlooked; therefore, this study has been planned to address this gap. **Objective:** To determine the risk factors for chronic kidney disease among young adult patients <40 years of age. **Method:** An unmatched case control study was conducted in district hospital in Madurai. The study compared patients with chronic kidney disease aged under 40 (cases) from the Nephrology ward and outpatient with similar-aged controls without CKD from the Medicine ward, using routine eGFR calculations for diagnosis. The calculated sample size was 76, which was rounded up to 100 participants in both the case and control groups. Data collection was done by using semi-structured questionnaire. Univariate and multivariate analysis were used to predict the risk factors for young CKD patients. **Results:** The study predicted that rural population (OR-5.236, 95% CI-2.489- 11.014), family history of CKD (OR-29.590, 95% CI-3.351-261.243), hypertension (OR-5.005, 95% CI-2.014-12.437), history of taking alternative medicine (OR-5.136, 95% CI-1.745-15.117), and recurrent urinary tract infection (OR-11.460, 95% CI-2.288-57.444) were significantly associated risk factors for CKD. **Conclusion**: This study predicted hypertension, rural population, family history of CKD, history of recurrent urinary tract infection, alcohol consumption as significant risk factors for CKD. Hypertension, history of recurrent urinary tract infection, alcohol consumption were modifiable risk factors. By controlling these modifiable risk factors, the burden of CKD can be reduced. In addition this study predicted that, rural population was more vulnerable to CKD, so the screening service to these populations through primary health care approach is essential.

Keywords: Case control study, Chronic kidney disease, Risk factors, Young adults

Introduction:

Chronic Kidney Disease (CKD) is an emerging non-communicable disease that contributes significant burden in both developed and developing countries. As per the Kidney Disease Outcome Quality Initiative, CKD is defined as kidney damage or glomerular filtration rate (GFR) < 60ml/min/1.73 m^2 for three months or more, irrespective of the cause.[1]

The CKD prevalence has shifted over time due to changes in demographic trends and in part with an increase in hypertension and diabetes mellitus.[2] The global prevalence of CKD as per the Global Burden of

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Disease (GBD) study in 2017 was 9.1% (8.5% - 9.8%) and resulted in 35.8 million Disability-Adjusted Life Years (DALYs), whereas 25.3 million of the Cardio Vascular Disease (CVD) DALYs could be attributed to impaired kidney function and mortality increased by 41.5%.[3] In 2020, a report from the International Society of Nephrology stated that CKD prevalence in men and in women was 10.4% and 11.8%, respectively.[4]

In India, there is no national data of the magnitude of CKD until 2005. This led to the formulation of the Indian CKD registry by the Indian Society of Nephrology to enroll all CKD patients. The prevalence of CKD in India is about 800 per million populations (pmp), while the incidence of End Stage Renal Disease (ESRD) is 150-200 pmp.[5] Screening and Early Evaluation of Kidney Disease Project (SEEK), an Indian cohort study conducted between 2005-2007, reported a 17.2% prevalence of CKD in the study cohort.[6] The prevalence of CKD in young adults varies from 7% - 22.27%.[7]

Less than 5% of the CKD patients are adolescents and young adults whose ten-year survival ranges from 70-85%.[7] Young adults with CKD leads poor quality of life (QoL) as they tend to face issues like unemployment, sickness absenteeism, discordant relationship, social isolation. This, in turn, leads them to psychological disturbance.[8] Their mortality rate is 30 times higher than their healthy peers.[7]

CKD is a one of the major causes of out-of-pocket health expenditure. As of 2017, more than 2.5 million people received renal replacement therapy, and this number is expected to double by 2030. Renal replacement therapy remains inaccessible in many developing countries owing to its cost. Approximately 2.37.1 million adults are expected to die prematurely from lack of access to renal replacement therapy.[9]

Huge burden of CKD is found to be due to their close association with diabetes and hypertension.[10] Apart from modifiable risk factors like diabetes, hypertension, smoking, alcohol, use of analgesic and alternative medicine, exposure to occupational hazards, kidney stones, non-modifiable risk factors like old age, race, gender, family history of CKD also contribute to the development of CKD.[11-15] This higher prevalence of CKD risk factors like hypertension and diabetes in the younger population necessitates a screening program for early detection in turn facilitates lifestyle modification and control of disease progression. Delayed diagnosis and treatment increase the risk of End Stage Renal Disease, cardiovascular complications leading to premature death. The screening program and guidelines for early identification of CKD among the younger population are often lacking in India. Hence, this study needed to explore the risk factors for CKD in the younger age group.

Objective:

To identify the risk factors for chronic kidney disease among young adult patients <40 years of age attending a tertiary care hospital in Madurai.

Method:

Study design: An unmatched case-control study

Study Site: Tertiary care hospital of Madurai district, Tamil Nadu during the period of October 2020 to December 2021

Study Population:

Inclusion Criteria:

Cases: Newly diagnosed chronic kidney disease patients which was confirmed by nephrologist, aged less than 40 years attending nephrology OP and ward were considered as cases

Controls: Patients without Chronic Kidney Disease and belong to the age same group admitted to the medicine ward on the day of data collection were considered as controls.

CKD in controls was diagnosed by calculating estimated GFR from age, height, weight, and serum creatinine (Cockcroft-Gault equation CrCl= 140-age*weight in kg/serum creatinine * 72) value obtained from the laboratory reports, which is done routinely for all inpatients.

Exclusion Criteria:

Unstable patients, Conditions causing acute kidney injury and congenital disorder of kidney, not willing to participate in the study were excluded from this study.

Sample size:

Sample size was calculated based on Palo SK et al[16] study by using following parameters with Confidence interval-95%, Power-80%, Ratio of control to case-1, Exposure among cases P1- 9.9% Exposure among controls P2- 0.01% P = 0.0989. Calculated Sample size was 76 and which was rounded up to 100 participants in both the case and control groups.

Sampling method:

Consecutive sampling method.

Study tool:

Data was collected by using pre-designed semi-structured questionnaire and Measurements like blood pressure, weight, height. The questionnaire of the present study was divided into two parts. Part 1consists of questionnaires regarding Socio-demographic details like age, sex, occupation, education, income and Part 2 consists of questionnaires to assess the risk factors like Family history of chronic kidney disease, medical history regarding co-morbidities like DM, HTN and frequency of Smoking habit, Alcohol consumption, History of taking native medicines, analgesic drugs, Previous history of treatment for recurrent urinary tract infection and renal stones.

Data collection method:

Data collection was done in the study area after obtaining permission from the Institute Ethics Committee.

a) Data was collected by the consecutive sampling method.

b) After obtaining informed consent, relevant information was obtained from the respondent using the semi-structured questionnaire in the local language.

c) Confidentiality maintained throughout the study period

Operational Definition:

The socio-economic status of the study participants was calculated by Modified Kuppusamy's socio-economic status scale 2020.

Body Mass Index is defined as the body mass (weight) divided by the square of the body height. It is expressed in units of kg/m^2.

Patients were interviewed regarding the use of alternative medicine during their lifetime and the preceding one year and duration of use.[17]

Regular use of analgesic intake was defined as taking analgesic or antipyretic tablets for fever or pain relief at least once a week over a consecutive period of 3 months.[17]

Recurrent urinary tract infection is defined as three or more UTIs within 12 months or two or more occurrences within six months. [18]

History of recurrent UTI in study participants was confirmed by taking medical treatment or getting admitted for treatment of UTI.

The previous history of kidney stones in study participants was confirmed by taking medical management or undergoing any surgical procedure for the same.

According to U.S. Food and Nutrition Board and the United Kingdom, the National health service recommends daily water intake for Indian males and

females should be 3.150 liters and 2.5 liters, respectively.[19] Study participants were interviewed about the amount of water intake (In Cases-before the diagnosis of CKD). Those who consume less than 2.5 liters were considered as inadequate water intake.

As per WHO, the daily recommended salt intake is 5 grams per day. Based on surveys done in various regions of India, salt intake among them varies from >6.5/g/day to 11 g/day.[19] Diets with significant contribution to high salt intake in our Indian settings are pickles, pappadams, hot spicy rasam, dry fish. Using food frequency method, the data was collected among the study participants.

Data Entry and Analysis

Google form was used for Data collection and the data was retrieved in an Excel format. Analysis of the data was carried out using SPSS Software version 20 (licensed). Descriptive statistics were used to find out the frequencies and percentages. Binary logistics and multiple logistic regression analysis were used to find the CKD predictors. p-value < 0.05 was considered as statistically significant.

Results :

In this study 68% belonged to the age group 30-40 years. Majority (86%) of the cases were in stage 5, followed by stage 4 (9%) and stage 3 (5%). Among the cases, 63% were males, whereas in controls 50% were males, and 50% were females. Based on the Modified Kuppusamy scale for socio-economic status, more than half of the study population belonged to class IV (50.5%), and 32% were unemployed. The majority of the study participants were married (90%) and following Hinduism as religion (89%). 18% of the cases had a family history of CKD, whereas only 1% of the controls had a positive family history. 16% of the cases had diabetes mellitus, and 22% of the controls had diabetes mellitus. The proportion of hypertension was higher among the cases (29%) than controls (9.1%). Among the cases, 20% had a history of taking alternative medicine, and in controls, it was only 7%. 21% of the cases had a history of analgesic abuse, and in controls 13% had history of analgesic abuse. A higher incidence of recurrent urinary tract infection was reported in cases (20%) than controls (2%). The proportion of cases (10%) with a history of treatment for renal stones was nearly similar to that of controls (9%). Among the cases, 35% were smokers, 65% were nonsmokers, whereas in controls, 26% were smokers, and 74% were nonsmokers. 37% of the cases and 20% of the controls were alcoholics. The proportion of cases with a history of salty food intake was slightly higher in controls (26%) than cases (20%). 63% of the cases consumed less than the recommended level of water (< 2.5 liters/day), whereas, in controls, only 58% consumed less than the recommended level of water.

Table 1 shows an association between risk factors and CKD by binary logistic regression by calculating unadjusted odds ratio indicates that family history of chronic kidney disease (OR-21.732, 95% CI, 2.840- 166.268) is the significant non-modifiable risk factor of chronic kidney disease among the selected patients. The CKD risk among those from rural areas was 4.6 times higher than those from urban areas, and the hypertensive patients had four times higher risk than normotensives. Other risk factors like recurrent urinary tract infection (OR-12.250, 95% CI, 2.780-53.989), history of taking alternative drugs (OR-3.321, 95% CI, 1.335- 8.261), consumption of alcohol (OR-2.349, 95% CI, 1.243- 4.439) showed a statistically significant association with CKD. Compared to the younger age group (18-29 years), the older age group 30-40 years had 1.3 times higher risk of developing CKD, but it was not statistically significant. Similarly, male gender (OR-1.703, 95% CI, 0.968- 2.994), use of analgesic medication (OR-1.779, 95% CI, 0.835- 3.788), history of renal stones

Table 1 : Association between Risk factors and CKD by Binary Logistic Regression [N=200]

Risk factors	Case (n=100)	Controls (n=100)	Total (n=200)	p-value	Odds ratio	95% CI
Age in Years						
18-29	29	35	64			Ref.
30-40	71	65	136	0.364	1.318	0.726 - 2.393
Gender						
Male	63	50	113	0.065	1.703	0.968 - 2.994
Female	37	50	87			Ref.
Marital status						
Married	88	92	180	0.349	0.638	0.249 - 1.634
Unmarried	12	8	20			Ref.
Residence						
Rural	75	39	114	0.000	4.692	2.562 - 8.595
Urban	25	61	86			Ref.
Family H/O CKD						
Yes	18	1	19	0.003	21.732	2.840-166.268
No	82	99	181			Ref.
Diabetes Mellitus						
Yes	16	22	38	0.281	0.675	0.331-1.379
No	84	78	162			Ref.
Hypertension						
Yes	29	9	38	0.001	4.13	1.838 -9.281
No	71	91	162			Ref.
H/O Taking alternative medicine						
Yes	20	7	27	0.010	3.321	1.335 -8.261
No	80	93	173			Ref.
Analgesic abuse						
Yes	21	13	34	0.135	1.779	0.835 -3.788
No	79	87	166			Ref.
Recurrent urinary tract infection						
Yes	20	2	22			Ref.
No	80	98	178	0.001	12.25	2.780 -53.989
H/o Treatment for Renal stones						
Yes	10	9	19			Ref.
No	90	91	181	0.81	1.123	0.436 - 2.895
H/o Smoking						
Yes	35	26	61	0.168	1.533	0.835 - 2.812
No	65	74	139			Ref.
H/O Alcohol consumption						
Yes	37	20	57	0.009	2.349	1.243 - 4.439
No	63	80	143			Ref.
Salty food intake						
Yes	26	20	46			Ref.
No	74	80	154	0.314	1.405	0.724- 2.728
Daily Water intake						
<2.5 L	63	58	121			Ref.
>3 L	37	42	79	0.47	1.233	0.699-2.176

Table 2 : Association between Risk factors and CKD by Multiple Logistic Regression [N=200]

Risk factors	Case (n=100)	Control (n=100)	Total (n=200)	p-value	Adjusted Odds ratio	95% CI
Residence						
Rural	75	39	114	0.000	5.236	2.489 – 11.014
Urban	25	61	86			Ref.
Family H/O CKD						
Yes	18	1	19	0.002	29.59	3.351-261.243
No	82	99	181			Ref.
Hypertension						
Yes	29	9	38	0.001	5.005	2.014 – 12.437
No	71	91	162			Ref.
H/O taking alternative medicine						
Yes	20	7	27	0.003	5.136	1.745 –15.117
No	80	93	173			Ref.
Recurrent urinary tract infection						
Yes	20	2	22	0.003	11.46	2.286-57.444
No	80	98	178			Ref.
H/O Alcohol consumption						
Yes	37	20	57	0.093	1.976	0.894-4.371
No	63	80	143			Ref.

(OR-1.123, 95% CI, 0.436- 2.895), smoking OR-1.533, 95% CI, 0.835- 2.812), reduced water intake (OR-1.233, 95% CI, 0.699-2.176) posed a higher risk of getting of CKD than their counterpart, but all these were not statistically associated.

Table 2 shows the association between CKD and various risk factors using multiple logistic regression. In binary logistic regression analysis, the following risk factors, family history of CKD, cases from the rural areas, hypertension, history of taking alternative drugs, history of recurrent urinary tract infection, alcohol consumption were significantly associated with CKD. Factors that are statistically significant in binary logistic regression were analysed in multivariate logistic regression, and adjusted odds ratios were calculated. The risk of developing CKD is 5.2 times (OR-5.236, 95% CI, 2.489-11.014) higher in the rural population, 29.6 times (OR-29.590, 95% CI, 3.351-261.243) higher among those with a family history of CKD. Cases with a history of taking alternative medicine had 5.1 times (OR-5.136, 95% CI, 1.745-15.117) higher risk than those without a history of taking alternative medicine. CKD risk among hypertensive patients is five times (OR-5.005, 95% CI, 2.014-12.437) higher than normotensive patients. Those with a history of recurrent urinary tract infection 11 times (OR-1.460, 95% CI, 2.286-57.444) higher risk of getting CKD than others.

Discussion:

The Mean age of the study participants was 32.2 $\pm$ 6.35 years. More than half of the study participants 113 (56.5%) were males. There were a slightly higher percentage of men among the cases in this study (63%). Similar findings were reported in a case-control study conducted in India (55.1%), Saudi Arabia (65%) and Egypt (61%).[6,20,21] In contrast, Suleymalar G et al[22] (18.4% in females, 12.8% in males) study showed a female predominance.

In this study, the rural setting was associated with increased odds (OR- 5.236, 95% CI, 2.489-11.014) of CKD. This is in concordance with the study

done in selected cities in India (Delhi, Haryana, Andra Pradesh, Tamil Nadu).[23] This might suggest that exposure to agricultural work and agrochemicals, a potential risk factor for CKD, which may be greater in rural populations.

In this study, CKD risk was higher among those who had a family history of CKD (OR-29.590). Similar to this study, a statistically significant association (5.2%, p-value- 0.001) was found in study conducted in Andra Pradesh.[24]

The increasing trend of non-communicable diseases among the general population due to urbanization and lifestyle modification justify the higher prevalence of diabetes (22%) among the controls in the current study. In this study, Diabetes had no significant association with CKD. Many Studies were predicted diabetes was a significant risk factor for CKD.[14,24]

Hypertension is considered as a risk factor and complication of CKD. The present study predicted that the odds of developing CKD among the patients with hypertension was approximately five times higher than those without hypertension, and it was statistically significant (p-value 0.001, (OR- 5.005, 95% CI, 2.014-12.437) which is similar to studies in India by Kanyari et al.[24] (p-value-<0.001), Kokila et al.[25] (OR-1.42) studies from India found a significant association between hypertension and CKD.

In this study, the CKD risk was 5.1 times higher in those who had a previous history of taking alternative medicine which was similar to study done by Akkilagunta et al.[17] (OR-5.15, 95% CI-1.27-20.87).

Present study found an increased risk of CKD (odds ratio-1.779) among those who had a history of analgesic intake for a longer period, though it was not statistically significant. A study done in Barcelona by Ibeiez et al.[26] showed an approximately similar risk of CKD (odds ratio-1.22) on prolonged use of any analgesic.

A significant association between the history of recurrent urinary tract infection with CKD was observed in this study [odds ratio -11.460, CI (2.286-57.444)]. Sajid et al.[14] study in Pakistan showed that urinary tract infection was a significant risk factor for CKD odds ratio- 2.213, CI (0.0848 5.778).

In this study, Alcoholics had 1.976 times higher risk than of non- alcoholics which was statistically significant. Similar to this study, Kokila et al.[25] (p-value-0.018) study found a significant association between alcohol consumption and CKD.

An ICMR case-control study by Palo SK in Odisha observed a higher prevalence of CKD among those who consume locally made alcohol (OR-1.091, 95% CI- 1.02 1.17).[16]

In this study, smokers posed a 1.5 times higher risk for CKD than nonsmokers, though it was not statistically significant. In contrast to our study, Kokila et al.[25] (OR-3.179, 95% CI 1.779-5.678) study found a significant association between smoking and CKD.

This study observed that those who consumed water less than 2.5 Liter per day had a higher risk for CKD (unadjusted OR-1.223) than those who consumed more water. A similar finding was obtained in Sontrop JM et al.[27] study [OR-2.52, 95% CI- (0.91 6.96)], the risk of developing CKD was more in low water intake groups

There was no significant association noticed between CKD and renal stones in this current study (p-value-0.810, OR-1.123), even though CKD risk was slightly higher in those who had a history of taking treatment for renal stones.

Nephrolithiasis is documented as a risk factor for CKD in Vupputuri S et al.[28] study. The present study was not observed a significant association (p-value-0.314, OR-1,405) between high salt intake and CKD because both cases and controls desired to eat salty food.

Conclusion:

This study predicted hypertension, rural population, family history of CKD, history of recurrent urinary tract infection, alcohol consumption as significant risk factors for CKD. Hypertension, history of recurrent urinary tract infection, alcohol consumption were modifiable risk factors. By controlling these modifiable risk factors, the burden of CKD can be reduced. In addition this study predicted that, rural population was more vulnerable to CKD, so the screening service to these populations through primary health care approach is essential.

Recommendations:

Need of awareness program regarding the CKD and their associated risk factors, health education regarding lifestyle modification including a healthy diet, physical activity and avoidance of alcohol, smoking cessation. Conducting training and education modules for Primary Health Centre physicians regarding screening, management, and timely referral of CKD patients. Mobile health education services like Kilkari for ANC mothers could be initiated for CKD to deliver messages about risk factors, management for minor ailments, conditions requiring admission for CKD. Emergence of CKD of unknown etiology in younger populations needs further research in blind spots like occupational exposure, water quality, and indigenous medicine leading to CKD.

Limitations:

This study was conducted in one hospital in Madurai district, and most of them belong to the lower socio-economic class, which limits its generalization to the whole community. It requires a community-based study to find the true prevalence of CKD and its associated risk factor among young adults. Bias could have happened due to inaccurate recall of past events

Declaration:

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Conflicts of interest: Nil

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