https://doi.org/10.48047/AFJBS.6.13.2024.6910-6926

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Assessing the Impact of Cultural, Socio-Economic, and Health Disparities on Chronic Kidney Disease: A Case-Control Study in Uddanam, Andhra Pradesh

Hari Ram Pampana[1], Sadguri Addanki[1], Dhanunjaya Varma Lakkamraju[1], John Dogulas Palleti[2], Sudhakar Godi[1], Paddaiah Gangisetti[1*]

[1]Department of Human Genetics, Andhra University, Visakhapatnam, A.P, India – 530003.

[2]Research and Development, Centre for Computational and Biological Sciences (CCBS),

48-12-17, Srinagar, Near RTC complex, Visakhapatnam-530016, Andhra Pradesh, India.

***Corresponding Author:** Paddaiah Gangisetti, Email: gpaddaiah@gmail.com

Volume 6, Issue 13, Aug 2024

Received: 15 June 2024

Accepted: 25 July 2024

Published: 15 Aug 2024

doi: 10.48047/AFJBS.6.13.2024.6910-6926

ABSTRACT

Chronic kidney disease (CKD) is a growing concern in both developed and developing nations worldwide. This study investigates the impact of cultural, socio-economic, and health factors on the prevalence and severity of CKD in the Kaviti and Kanchili areas within the Uddanam region of North Coastal Andhra Pradesh, India. A retrospective analysis was conducted on 2,806 participants. Statistical methods, including the Chi-square test, Student's t-test, and Binary Logistic Regression analysis, were employed to assess the associations between selected parameters and CKD. The findings indicate that residing in rural areas and having a lower socio-economic status significantly contribute to the development of CKD. Moreover, patients with CKD are incurring higher medical expenses as the disease progresses. There is an urgent need to improve healthcare facilities, particularly those specializing in kidney diseases, and to raise awareness about CKD risk factors.

Keywords: Chronic kidney disease, CKDu, Cultural, Socio-economic.

INTRODUCTION

Chronic kidney disease (CKD) is a significant public health issue that profoundly impacts society. It affects over 10% of the global population and approximately 17.2% of the adult population in India (Kovesdy, 2022; Singh et al., 2013). Globally, CKD is prevalent among patients with comorbid conditions such as hypertension and diabetes (Alemu et al., 2020). However, another form of CKD, primarily reported in rural populations, affects individuals who are typically non-diabetic and have mild hypertension, yet develop chronic kidney failure. This variant, known as CKD of unknown etiology (CKDu) (Anupama et al., 2020), has been documented in various regions, including the Pacific coast areas of Central America, El Minya Governorate in Egypt, the North Central Province of Sri Lanka, and the Uddanam region and Chimakurthy mandals in Andhra Pradesh, India (Keogh et al., 2022; Gifford et al., 2017; Rajapakse et al., 2016; Tatapudi et al., 2019; Lal et al., 2020).

The Uddanam region, consisting of seven mandals in the Srikakulam district of Andhra Pradesh, is renowned for its cashew and coconut cultivation. This region bears a significant burden of CKD of unknown etiology (CKDu), with an estimated 34,000 affected individuals and approximately 4,500 deaths (John et al., 2021). Andhra Pradesh has the highest prevalence of CKD in India at 46.8%. Recent surveys have indicated a CKD prevalence of 32.2% among male farm workers and 18.3% among other rural communities in Andhra Pradesh (Farag et al., 2020. Specifically, in the Uddanam areas of Kaviti and Kanchili, the incidence of CKDu is notably high, with 25.4% in Kaviti and 16-20% in Kanchili, rates significantly above the national average (Gummidi et al., 2020).

Over the past two decades, thousands of people in the Uddanam region have been affected by CKD, with many succumbing to the disease in their prime years. This has had devastating impacts on families, communities, and society at large. In developed countries, the annual expenses associated with end-stage renal disease range from $20,110 to $100,593 per patient, primarily due to the progression from CKD stage 3 to stages 4-5 (Elshahat et al., 2020). These medical expenses are considered "catastrophic health expenditures," often exceeding 30% of a family's total income. Ethnic minorities and individuals with low socioeconomic status in industrialized countries are disproportionately affected by CKD (Nicholas et al., 2015). Similarly, in industrializing countries like India and Mexico, the prevalence of CKD is high among socioeconomically disadvantaged populations (Robles-Osorio & Sabath, 2016).

Socioeconomic status (SES) is the most studied social determinant of CKD. SES, which measures social and economic well-being, is often assessed through four aspects: education, occupation, economic status, and habitat (Nicholas et al., 2015). Understanding these factors can aid in developing more effective kidney disease prevention programs for disadvantaged populations.

This study aims to assess the impact of cultural, socio-economic, and health disparities on the prevalence and severity of CKD in the Uddanam region. By conducting a case-control study with 2,806 participants, we seek to elucidate the associations between these factors and CKD, providing insights that can inform targeted interventions and policy decisions to address this pressing health challenge.

METERIALS AND METHODS

In this retrospective case-control study, 2,806 participants were recruited from two hotspot areas, Kaviti and Kanchili, in the Uddanam region, where CKD is widespread. The sample comprised 1,001 cases and 1,001 controls from Kaviti, and 404 cases and 404 controls from Kanchili.

Data were collected using pre-designed and tested schedules through personal interviews with both patients and controls, and further verified through interviews with other family members. Given the rural nature of the field areas, where travel facilities are inadequate and residents are often wary of strangers, significant efforts were made to gain their cooperation. This was achieved with the assistance of primary healthcare providers and Accredited Social Health Activist (ASHA) workers, who received instructions from state and district administrative and health officials.

Patient data, including information on comorbidities and diabetic status, were sourced from medical records available at Primary Health Centers. Participants were then approached for further information and details to ensure comprehensive data collection.

During the data collection process, the primary focus was on assessing cultural, social, and direct economic costs associated with CKD. Cultural characteristics, such as caste and sub-caste, education, occupation, economic category, and habitat, were categorized under social characteristics. The section on healthy family habits included variables like fasting, physical activity, and abstinence from tobacco and alcohol. Health conditions, including diabetes, blood pressure, and other chronic or acute health problems apart from CKD, were documented under health conditions.

The direct economic costs section captured expenses related to transportation to hospitals, diagnosis, medicines, dialysis, the duration of the CKD condition, and transplant. Additionally, the questionnaire assessed the extra burden on medical institutions, including Primary Health Centers (PHCs), Mandal headquarters, regional headquarters, and district headquarters.

The questionnaire used for interviewing CKD patients was approved by the ethical committees of the Indian Council of Medical Research (ICMR) and Andhra University.

The Udai Pareekh Socio-Economic Status Scale (Pareek U & Trivedi G, 1995) was employed to differentiate the economic levels of individuals, categorizing them as lower class (<13), middle class (24-32), and upper class (>43). Physical activity levels were assessed following the World Health Organization (WHO) recommendations, which define physical activity as movement produced by skeletal muscles that result in energy expenditure: 150–300 minutes of moderate-intensity aerobic physical activity or 75–150 minutes of vigorous-intensity aerobic physical activity per week.

Diabetes diagnosis was based on WHO criteria, with fasting plasma glucose ≥126 mg/dl (7.0 mmol/l) or 2-hour plasma glucose ≥200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test. Tobacco use was categorized into smokeless tobacco (Gutkha, panmasala, khaini) and tobacco smokers (bidi, cigarette, hookah).

Hypertension was measured following the 2017 American College of Cardiology/American Heart Association (ACC/AHA) blood pressure guidelines, classifying normal blood pressure as <130/80 mmHg, stage 1 hypertension as 130-139/80-89 mmHg, and stage 2 hypertension as ≥140/90 mmHg.

Alcohol consumption was assessed using the National Institute on Alcohol Abuse and Alcoholism (NIAAA) guidelines. Moderate alcohol use was defined as up to 2 drinks or less per day for men and 1 drink or less per day for women. Heavy alcohol use was defined as 15 or more drinks per week for men and 8 or more drinks per week for women.

Inclusion criteria:

Patients: Individuals hospitalized with chronic kidney disease who are registered in either government or private medical institutions, with a serum creatinine level >2 mg/dl and an estimated glomerular filtration rate (eGFR) < 60 mg/mmol.

Controls: Individuals residing near or beside the CKD patient's house who do not have any kidney-related illnesses.

Exclusion criteria:

Individuals who were misdiagnosed as kidney patients, those lacking specific biochemical reports, and those who had previously died from chronic kidney disease were excluded from the study.

Statistical analysis:

Logistic and multiple regression analyses, along with independent t-tests, were applied to measure the association between selected parameters, such as average monthly spending on transport, diagnosis, and medicine, in comparison to various parameters of CKD and normal subjects.

To measure the adjusted associations between categorical variables and CKD, the chi-square test was employed. Binary logistic regression was used to assess the adjusted associations between study variables and CKD. Additionally, R^2 values, odds ratios, and 95% confidence intervals were calculated. An independent t-test was utilized to compare the means of two variables. Results with a p-value ≤ 0.05 (two-sided) were considered statistically significant. All analyses were conducted using IBM® SPSS® version 25.

RESULTS

In the present study, both case and control groups had nearly equal percentages of males and females, with a slightly higher percentage of males compared to females. A higher percentage of participants belonged to the backward caste compared to other castes. Additionally, there were a higher number of illiterates, and a significant portion of the population was engaged in agriculture-related or manual work. Most participants lived in rural areas and fell into the lower economic status category.

Regarding the study population's lifestyle and health characteristics, a larger proportion consumed non-vegetarian food, chewed tobacco, and drank less alcohol. A significant percentage engaged in physical activity, while the habit of fasting was very low. There were fewer people with diabetes, but a higher number had high blood pressure compared to the control group.

In terms of morbidity, there were fewer individuals with short- and long-term conditions. Only a few participants had undergone dialysis or kidney transplants. The majority of those suffering from kidney disease had been affected for a period of 0-5 years (Figure 1).

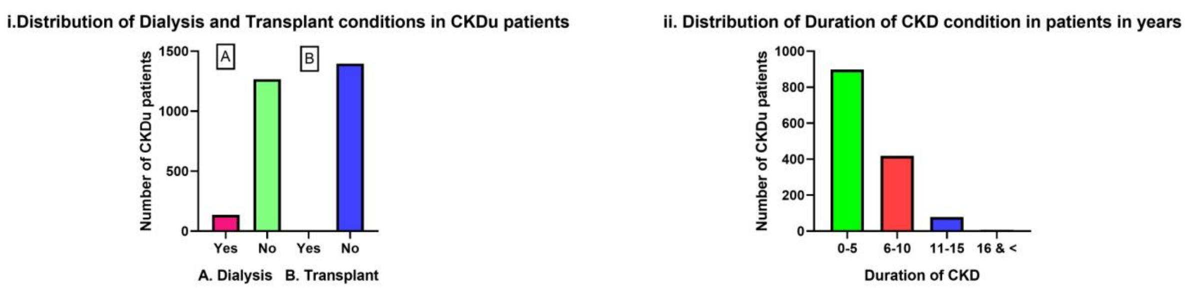

Figure 1. Distribution of dialysis, Transplant, duration of CKD in patients

The results of the Chi-square and t-test analyses are illustrated in Table 1. Chi-square analysis revealed that several variables, including caste system, education, occupation, economic category, physical activity, tobacco use, alcohol consumption, diabetes, hypertension, other ailments, and other chronic or acute health problems, were significantly associated with CKDu ($p < 0.05$).

The independent t-test analysis showed significant differences in means and variances between cases and controls for variables such as water intake, and costs of transport, diagnosis, and medicines.

Table 1. Unadjusted associations between cultural and socio-economic and health related variables with risk of CKDu.

variables	Kaviti		Kanchili		Kaviti and kanchili	
	Case N (%)	Control N (%)	Case N (%)	Control N (%)	Case N (%)	Control N (%)
Males	538 (53.74)	548 (54.74)	259 (64.42)	196 (48.75)	797 (56.8)	744 (53)
Females	463 (46.25)	453 (45.25)	143 (35.57)	206 (51.24)	606 (43.9)	659 (46.9)

I. Cultural variables Caste system **						
Back ward caste	858 (85.7)	817 (81.6)	326 (81.1)	383(95.3)	1184(84.4)	1200 (85.5)
Open category	12 (1.2)	7 (0.7)	34 (8.5)	3 (0.7)	46 (3.3)	10 (0.7)
Scheduled castes and tribes	131(13.1)	177(17.7)	42 (10.4)	16 (4.0)	173(12.3)	193 (13.8)
II. Social variables a. Education **						
Illiterate	687(68.6)	525 (52.4)	238 (59.2)	220 (54.7)	925(65.9)	913 (65.1)
Primary	183 (18.3)	7 (0.7)	90 (22.4)	47 (11.7)	273 (19.5)	47 (3.3)
High school	105 (10.5)	209 (20.9)	60 (14.9)	98 (24.4)	165 (11.8)	307(21.9)
College and above	26 (2.6)	99 (9.9)	14 (3.5)	37 (9.2)	40 (2.9)	136 (9.7)
b. Occupation **						
Manuel/agriculture labor	653 (65.2)	582 (58.1)	226 (56.2)	194 (48.3)	879 (62.7)	776 (55.3)
former	147 (14.7)	162 (16.2)	102 (25.4)	76 (18.9)	249 (17.7)	238 (17)
Petty business	20 (2)	30 (3)	5 (1.2)	14 (3.5)	25 (1.8)	44 (3.1)
Any other	181 (18.1)	227 (22.7)	69 (17.2)	118 (29.4)	250 (17.8)	345 (24.6)
c. Economic category **						
Lower	817 (81.6)	565 (56.4)	334 (83.1)	188 (46.8)	1151 (82)	753 (53.7)
Middle	184 (18.4)	426 (42.6)	66 (16.4)	212 (52.7)	250 (17.8)	638 (45.5)
Upper	0 (0.0)	10 (1)	2 (0.5)	2 (0.5)	2 (0.1)	12 (0.9)
III. Other variables i. life style a. food habit						
Non - vegetarian	25 (2.5)	27 (2.7)	11 (2.7)	7 (1.7)	1367 (97.4)	1369 (97.6)
vegetarian	976 (97.5)	974 (97.3)	391 (97.3)	395 (98.3)	36 (2.6)	34 (2.4)
b. Water intake **						
Independent t-test results	F= 2.939, t= -7.127		F=20.655, t= -3.306		F= 10.439, t = -7.81	
ii. Healthy habits of family a. Fasting						
Yes	89 (8.9)	108 (10.8)	35 (8.7)	26 (6.5)	124 (8.8)	134 (9.6)
No	912 (91.1)	893 (89.2)	367 (91.3)	376 (93.5)	1279 (91.2)	1269 (90.4)
b. Physical activities involment **						
Yes	988 (98.7)	992 (99.1)	376 (93.5)	398 (99)	1364 (97.2)	1390 (99.1)
No	13 (1.3)	9 (0.9)	26 (6.5)	4 (1)	39 (2.8)	13 (0.9)
c. Tobacco chewing **						
Yes	788 (78.7)	527 (52.6)	249 (61.9)	153 (38.1)	1037 (73.9)	680 (48.5)
No	213 (21.3)	474 (47.4)	213 (21.3)	474 (47.4)	366 (26.1)	723 (51.5)
d. Alcohol consumption **						
Yes	280 (28)	210 (21)	130 (32.3)	64 (15.9)	410 (29.2)	274 (19.5)
No	721 (72)	791 (79)	272 (67.7)	338 (84.1)	993 (70.8)	1129 (80.5)

iii. Health conditions a. diabetes *						
Yes	125 (12.5)	93 (9.3)	51 (12.7)	33 (8.2)	176 (12.5)	126 (9)
No	876 (87.5)	908 (90.7)	351 (87.3)	369 (91.8)	1227 (87.5)	1277 (91)
b. Hypertension **						
Yes	528 (52.7)	171 (17.1)	227 (56.5)	63 (15.7)	755 (53.8)	234 (16.7)
No	473 (47.3)	830 (82.9)	175 (43.5)	339 (84.3)	648 (46.2)	1169 (83.3)
c. Any other ailments **						
Yes	366 (36.6)	129 (12.9)	150 (37.3)	35 (8.7)	516 (36.8)	164 (11.7)
No	635 (63.4)	872 (87.1)	252 (62.7)	367 (91.3)	887 (63.2)	1239 (88.3)
d. any other chronic or acute health problem						
Yes	66 (6.6)	47 (4.7)	22 (5.5)	15 (3.7)	88 (6.3)	62 (4.4)
No	935 (93.4)	954 (95.3)	380 (94.5)	387 (96.3)	1315 (93.7)	1341 (95.6)
iv. Direct economic costs of CKD , their independent t- test results						
1. Transport to the hospital **	F= 336.234, t= 22.335		F= 87.109 , t= 11.843		F= 439.45, t= 24.86	
2. Diagnostics **	F= 482.422, t= 27.950		F= 278.274, t= 15.038		F= 756.13, t= 31.126	
3. Medicines **	F= 310.66, t= 33.249		F= 46.611, t= 14.311		F= 356.51, t= 35.439	

Note: * represents p = < 0.05 (5% level of significance), ** p = 0.001 (0.1% level of significance) and F= difference between variance, t = difference between mean.

The results of the logistic regression analysis, illustrated in Table 2, revealed significant associations between various factors and the risk of CKDu. In the cultural variables section, the caste system showed that individuals in the open category had a higher risk (OR O C/SC&ST = 5.132, 95% CI: 2.513-10.48). Among social variables, primary education level (OR PRIMARY/COLLEGE AND ABOVE = 3.246, 95% CI: 9.598-25.766) and occupation as farmers (OR FARMER/ANY OTHER = 1.620, 95% CI: 1.226-2.14) were significantly associated with CKDu. Lower economic status (OR LOWER/UPPER = 7.011, 95% CI: 1.482-33.17) was also a significant factor. In the health conditions section, hypertension (OR YES/NO = 5.088, 95% CI: 4.200-6.163) and other ailments (OR YES/NO = 3.714, 95% CI: 2.992-4.610) were significantly associated with the risk of CKDu. Physical activity was found to play a significant protective role against CKDu.

Table 2. Adjusted association between cultural and socio-economic and health related variables with risk of CKDu.

Variables	Kaviti	Kanchili	Kaviti and kanchili
	OR (95% -CI) , p-value	**OR (95% -CI) , p- value**	**OR (95% -CI) , p-value**
I. Cultural variables			

Caste system			
Back ward caste	1.419 (1.11-1.814) *	0.324 (0.179-0.588) **	1.101 (0.883-1.372)
Open category	2.316 (0.888-6.044)	4.317 (1.161-16.056)	5.132 (2.513-10.480) **
Scheduled castes and tribes	reference	reference	reference
II. Social variables **a. Education**			
High school	1.9 (1.143-3.15) **	1.407 (0.643-3.078)	1.750 (1.123-2.625) **
Illiterate	3.557 (2.213- 5.71) **	2.009 (0.957-4.215)	2.943 (1.482-3.267) **
Primary	3.444 (2.089-5.67) **	3.870 (1.738-8.619) **	3.246 (9.598-25.76) **
College and above	reference	reference	reference
b. Occupation			
former	1.330 (0.934-1.89) **	2.270 (1.404-3.671) **	1.620 (1.226-2.14) **
Manuel/agriculture labor	0.848 (0.648-1.10)	0.934 (0.613-1.423)	0.887 (0.710-1.109)
Petty business	0.898 (0.437-1.84)	0.773 (0.231-2.589)	0.949 (0.526-1.71)
Any other	reference	reference	reference
c. Economic category			
Lower	---	0.950 (0.079-11.445)	7.011 (1.482-33.17) **
Middle	---	0.142 (0.012-1.704)	1.654 (0.349-7.843)
Upper	---	reference	reference
III. Behavioral variables **i. life style** **a. food habit**			
Non - vegetarian	1.082 (0.624-1.878)	0.630 (0.242-1.642)	1.087 (0.618-1.91)
vegetarian	reference	reference	reference
ii. Healthy habits of family **a. Fasting**			
Yes	0.861 (0.632-1.172)	1.271 (0.729-2.218)	1.174 (0.873-1.578)
No	reference	reference	reference
b. Physical activities involment			
Yes	0.606 (0.248-1.483)	0.134 (0.046-0.396) **	0.449 (0.218-0.924) *
No	reference	reference	Reference
c. Tobacco chewing			
Yes	0.305 (0.249- 0.373) **	0.447 (0.326-0.611) **	0.351 (0.292-0.423) **
No	reference	reference	reference
d. Alcohol consumption			
Yes	0.938 (0.755-1.166)	0.569 (0.392-0.828) **	0.787 (0.640-0.968) **
No	reference	reference	reference
iii. Health conditions **a. diabetes**			
Yes	0.724 (0.522-1.004)	0.747 (0.431-1.295)	0.745 (0.559-0.994) *
No	reference	reference	reference
b. Hypertension			
Yes	5.060 (4.07-6.291) **	6.036 (4.224-8.625) **	5.088 (4.200-6.163) **
No	reference	reference	reference
c. Any other ailments			
Yes	3.266 (2.566-4.158)	4.77 (3.110-7.316) **	3.714 (2.992-4.610) **

	**		
No	reference	reference	reference
d. any other chronic or acute health problem			
Yes	1.049 (0.677-1.626)	1.37 (0.646-2.907)	1.023 (0.697-1.502)
No	reference	reference	reference

Note: * represents p = < 0.05 (5% level of significance), ** p = 0.001 (0.1% level of significance), CI – class intervals OR - Odd's Ratio, reference: baseline category.

DISCUSSION

The results of this study suggest that several factors, including the caste system, education, occupation, tobacco use, alcohol consumption, physical activity, blood pressure, and other ailments, may impact the risk of CKDu in the Uddanam region.

Our findings indicate that the caste system is significantly associated with the risk of CKDu, with those in the lower hierarchical levels, such as Scheduled Castes and Scheduled Tribes, being more prone to the disease (Palo et al., 2021). This aligns with previous studies showing a higher frequency of abnormal kidney function among lower caste groups. A possible reason for this increased risk could be the lack of knowledge about nutritious food and healthy habits, which is often correlated with poverty. This lack of awareness and resources may contribute to the higher susceptibility of these groups to CKDu.

In this study, education and occupation were found to be significantly associated with the risk of CKDu. Our findings on the impact of education align with a study conducted on multi-ethnic Asian populations in Singapore (Sabanayagam et al., 2010). Additionally, research from Sweden and India has suggested that individuals involved in manual or agricultural work, as well as unskilled workers, are at higher risk of developing CKD (Mohanty et al., 2020; Fored et al., 2003). In the Uddanam region, where one-third of the population is illiterate, lack of education emerges as a significant risk factor for CKDu, particularly among farmers and daily wage laborers engaged in paddy and cashew cultivation.

One of the variables, physical activity, was negatively associated with the risk of CKDu. This finding aligns with several other studies that suggest physical activity may protect against kidney disease. These studies have indicated that higher levels of physical activity are significantly associated with a lower prevalence of proteinuria in both men and women, and increased physical activity might offer a survival benefit for the CKD population (Stump, 2011; Koba, 2016; Beddhu et al., 2009). In the Uddanam region, a significant percentage of the population is engaged in physical activities, which appears to have a protective effect against CKDu.

Conversely, in the Uddanam region, where nearly half of the population engages in smoking or chewing tobacco, tobacco consumption emerged as a significant risk factor for CKDu. This finding is consistent with other studies that link smoking habits to an increased risk of CKD (Huda et al., 2012). Additionally, alcohol consumption, particularly of locally made alcohol, was associated with CKDu risk (Palo et al., 2021; Sabanayagam et al., 2010). This supports previous research suggesting that individuals who consume locally made alcohol and habitual drinkers are at an elevated risk of CKDu. However, in this region, fewer individuals exhibit alcohol consumption habits, with a notable prevalence of male individuals consuming mild alcoholic beverages derived from palm trees.

Another significant finding of the current study is the association between hypertension and the risk of CKDu. This result is consistent with several other studies that suggest a history of hypertension increases the risk of developing CKD (Sabanayagam et al., 2010). In the Uddanam region, nearly half of the population is hypertensive, making hypertension a critical factor that may accelerate the progression of CKD to End-Stage Renal Disease (ESRD).

Additionally, our study found various comorbidities to be significantly associated with CKDu risk. In the Uddanam region, gastric abnormalities, eye abnormalities, thyroid disorders, and asthma were the predominant ailments observed among CKDu patients, which is consistent with findings from other studies. These studies have indicated that hemodialysis patients have an elevated risk of upper gastrointestinal bleeding compared to the general population, retinopathy can affect kidney function, hypothyroidism is a risk factor for CKD and its progression, and asthma patients are at risk of developing CKD (Kuo et al., 2013; Grunwald et al., 2012; Rhee, 2016; Huang et al., 2014). However, in this region, there was a lower frequency of patients presenting with these additional ailments alongside CKD.

A significant difference in water intake was observed between the case and control groups. This finding aligns with other studies that have shown lower total water intake is associated with chronic kidney disease, and increased water intake may benefit kidney function (Sontrop et al., 2013; Clark et al., 2013). Additionally, significant differences were observed in the costs of transport to the hospital, diagnosis, and medicine between cases and controls. Our analysis indicates that as the severity of the disease increases, the medical expenses also rise. Patients with stage 4 and stage 5 CKDu spend more money on treatment than those with stage 3 and stages 1 & 2 CKDu compared to controls.

These findings are consistent with other studies that highlight the substantial financial impact of CKD, particularly due to high costs related to renal replacement therapy (RRT) and cardiovascular complications. The direct and indirect societal costs of CKD and end-stage renal disease are significant and escalate as the disease progresses (Kerr et al., 2012; Wang et al., 2016). In the Uddanam region, patients' average monthly spending on medicines in both areas is nearly Rs. 3000, which imposes a substantial financial burden on them.

CONCLUSION

Our study underscores the significant influence of various factors on the prevalence of Chronic Kidney Disease of Unknown Etiology (CKDu) in the Uddanam region. Socioeconomic disparities, lifestyle behaviors such as tobacco and alcohol consumption, hypertension, and comorbidities including gastric abnormalities and asthma were all associated with an increased risk of CKDu. Conversely, physical activity emerged as a protective factor, while lack of education and lower caste status were identified as key determinants of CKDu susceptibility. These findings highlight the complex interplay of social, economic, and health factors in the development of CKDu. Moving forward, targeted interventions that address these factors are essential to reduce CKDu prevalence and alleviate its burden on affected individuals and healthcare systems.

ACKNOWLEDGEMENTS

This paper is part of an Ad hoc Major Research Project funded by Indian council of medical research (ICMR), New Delhi, India (Letter No: Adhoc / 189 /2020 /SBHSR).

Ethics approval and consent to participate:

Informed consent was obtained from all subjects and/or their legal guardian(s). Andhra University Institutional Ethical committee has reviewed and approved the study protocol (Approval No. IEC 42 / 22 - 06 – 2020).

Declaration of Conflicting Interests:

The authors declare that there is no conflict of interest associated with authorship, and/or publication of this manuscript.

REFERENCES

1. Alemu, H., Hailu, W., & Adane, A. (2020). Prevalence of Chronic Kidney Disease and Associated Factors among Patients with Diabetes in Northwest Ethiopia: A Hospital-Based Cross-Sectional Study. *Current Therapeutic Research*, 92, 100578. https://doi.org/10.1016/j.curtheres.2020.100578
2. Anupama, Y. J., Sankarasubbaiyan, S., & Taduri, G. (2020). Chronic kidney disease of unknown etiology: Case definition for India – A perspective. *Indian Journal of Nephrology*, 30(4), 236. https://doi.org/10.4103/ijn.ijn_327_18
3. Beddhu, S., Baird, B. C., Zitterkoph, J., Neilson, J., & Greene, T. (2009). Physical Activity and Mortality in Chronic Kidney Disease (NHANES III). *Clinical Journal of the American Society of Nephrology*, 4(12), 1901–1906. https://doi.org/10.2215/cjn.01970309
4. Clark, W. F., Sontrop, J. M., Huang, S. H., Gallo, K., Moist, L., House, A. A., Weir, M. A., & Garg, A. X. (2013). The chronic kidney disease Water Intake Trial (WIT): results from the pilot randomised controlled trial. *BMJ Open*, 3(12), e003666. https://doi.org/10.1136/bmjopen-2013-003666
5. Elshahat, S., Cockwell, P., Maxwell, A. P., Griffin, M., O'Brien, T., & O'Neill, C. (2020). The impact of chronic kidney disease on developed countries from a health economics perspective: A systematic scoping review. *PLoS ONE*, 15(3), e0230512. https://doi.org/10.1371/journal.pone.0230512
6. Farag, Y. M. K., Subramanian, K. K., Singh, V. A., Tatapudi, R. R., & Singh, A. K. (2020). Occupational risk factors for chronic kidney disease in Andhra Pradesh:

'Uddanam Nephropathy.' *Renal Failure*, 42(1), 1032–1041. https://doi.org/10.1080/0886022x.2020.1824924

7. Fored, C. M., Ejerblad, E., Fryzek, J. P., Lambe, M., Lindblad, P., Nyrén, O., & Elinder, C. G. (2003). Socio-economic status and chronic renal failure: a population-based case-control study in Sweden. *Nephrology Dialysis Transplantation*, 18(1), 82–88. https://doi.org/10.1093/ndt/18.1.82
8. Gifford, F. J., Gifford, R. M., Eddleston, M., & Dhaun, N. (2017). Endemic Nephropathy Around the World. *Kidney International Reports*, 2(2), 282–292. https://doi.org/10.1016/j.ekir.2016.11.003
9. Grunwald, J. E., Alexander, J., Ying, G. S., Maguire, M., Daniel, E., Whittock-Martin, R., Parker, C., McWilliams, K., Lo, J. C., Go, A., Townsend, R., Gadegbeku, C. A., Lash, J. P., Fink, J. C., Rahman, M., Feldman, H., Kusek, J. W., Xie, D., & Jaar, B. G. (2012). Retinopathy and Chronic Kidney Disease in the Chronic Renal Insufficiency Cohort (CRIC) Study. *Archives of Ophthalmology*, 130(9), 1136. https://doi.org/10.1001/archophthalmol.2012.1800
10. Gummidi, B., John, O., Ghosh, A., Modi, G. K., Sehgal, M., Kalra, O. P., Kher, V., Muliyil, J., Thakur, J. S., Ramakrishnan, L., Pandey, C. M., Sivakumar, V., Dhaliwal, R. S., Khanna, T., Kumari, A., Prasadini, G., Reddy, J. C., Reddy, J., & Jha, V. (2020). A Systematic Study of the Prevalence and Risk Factors of CKD in Uddanam, India. *Kidney International Reports*, 5(12), 2246–2255. https://doi.org/10.1016/j.ekir.2020.10.004
11. Huang, H. L., Ho, S. Y., Li, C. H., Chu, F. Y., Ciou, L. P., Lee, H. C., Chen, W. L., & Tzeng, N. S. (2014). Bronchial asthma is associated with increased risk of chronic kidney disease. *BMC Pulmonary Medicine*, 14(1). https://doi.org/10.1186/1471-2466-14-80
12. Huda, M. N., Alam, K. S., & Harun-Ur-Rashid, N. (2012). Prevalence of Chronic Kidney Disease and Its Association with Risk Factors in Disadvantageous Population. *International Journal of Nephrology*, 2012, 1–7. https://doi.org/10.1155/2012/267329
13. John, O., Gummudi, B., Jha, A., Gopalakrishnan, N., Kalra, O. P., Kaur, P., Kher, V., Kumar, V., Machiraju, R. S., Osborne, N., Palo, S. K., Parameswaran, S., Pati, S., Prasad, N., Rathore, V., Rajapurkar, M. M., Sahay, M., Tatapudi, R. R., Thakur, J. S., . . . Jha, V. (2021). Chronic Kidney Disease of Unknown Etiology in India: What Do We Know and

Where We Need to Go. *Kidney International Reports*, 6(11), 2743–2751. https://doi.org/10.1016/j.ekir.2021.07.031

14. Keogh, S. A., Leibler, J. H., Decker, C. M. S., Velázquez, J. J. A., Jarquin, E. R., Lopez-Pilarte, D., Garcia-Trabanino, R., Delgado, I. S., Petropoulos, Z. E., Friedman, D. J., Sánchez, M. R. A., Guevara, R., McClean, M. D., Brooks, D. R., & Scammell, M. K. (2022). High prevalence of chronic kidney disease of unknown etiology among workers in the Mesoamerican Nephropathy Occupational Study. *BMC Nephrology*, 23(1). https://doi.org/10.1186/s12882-022-02861-0
15. Kerr, M., Bray, B., Medcalf, J., O'Donoghue, D. J., & Matthews, B. (2012). Estimating the financial cost of chronic kidney disease to the NHS in England. *Nephrology Dialysis Transplantation*, 27(suppl_3), iii73–iii80. https://doi.org/10.1093/ndt/gfs269
16. Koba, S. (2016). Physical Activity and Chronic Kidney Disease. *Journal of Atherosclerosis and Thrombosis*, 23(4), 395–396. https://doi.org/10.5551/jat.ed039
17. Kovesdy, C. P. (2022). Epidemiology of chronic kidney disease: an update 2022. *Kidney International Supplements*, 12(1), 7–11. https://doi.org/10.1016/j.kisu.2021.11.003
18. Kuo, C. C., Kuo, H. W., Lee, I. M., Lee, C. T., & Yang, C. Y. (2013). The risk of upper gastrointestinal bleeding in patients treated with hemodialysis: a population-based cohort study. *BMC Nephrology*, 14(1). https://doi.org/10.1186/1471-2369-14-15
19. Lal, K., Sehgal, M., Gupta, V., Sharma, A., John, O., Gummidi, B., Jha, V., & Kumari, A. (2020). Assessment of groundwater quality of CKDu affected Uddanam region in Srikakulam district and across Andhra Pradesh, India. *Groundwater for Sustainable Development*, 11, 100432. https://doi.org/10.1016/j.gsd.2020.100432
20. Mohanty, N. K., Sahoo, K. C., Pati, S., Sahu, A. K., & Mohanty, R. (2020). Prevalence of Chronic Kidney Disease in Cuttack District of Odisha, India. *International Journal of Environmental Research and Public Health*, 17(2), 456. https://doi.org/10.3390/ijerph17020456
21. Nicholas, S. B., Kalantar-Zadeh, K., & Norris, K. C. (2015). Socioeconomic Disparities in Chronic Kidney Disease. *Advances in Chronic Kidney Disease*, 22(1), 6–15. https://doi.org/10.1053/j.ackd.2014.07.002
22. Palo, S. K., Swain, S., Chowdhury, S., & Pati, S. (2021). Epidemiology & attributing factors for chronic kidney disease: Finding from a case–control study in Odisha, India.

The Indian Journal of Medical Research, 154(1), 90. https://doi.org/10.4103/ijmr.ijmr_2148_18

23. Pareek, U. and Trivedi, G. (1995) Manual of Socio-Economic Status Scale (Rural). *Manasayan Publishers*, New Delhi.
24. Rajapakse, S., Shivanthan, M. C., & Selvarajah, M. (2016). Chronic kidney disease of unknown etiology in Sri Lanka. *International Journal of Occupational and Environmental Health*, 22(3), 259–264. https://doi.org/10.1080/10773525.2016.1203097
25. Rhee, C. M. (2016). The interaction between thyroid and kidney disease: an overview of the evidence. *Current Opinion in Endocrinology Diabetes and Obesity*, 23(5), 407–415. https://doi.org/10.1097/med.0000000000000275
26. Robles-Osorio, M. L., & Sabath, E. (2016). Disparidad social, factores de riesgo y enfermedad renal crónica. *Nefrología*, 36(5), 577–579. https://doi.org/10.1016/j.nefro.2016.05.004
27. Sabanayagam, C., Lim, S. C., Wong, T. Y., Lee, J., Shankar, A., & Tai, E. S. (2010). Ethnic disparities in prevalence and impact of risk factors of chronic kidney disease. *Nephrology Dialysis Transplantation*, 25(8), 2564–2570. https://doi.org/10.1093/ndt/gfq084
28. Singh, A. K., Farag, Y. M. K., Mittal, B. V., Subramanian, K. K., Reddy, S. R. K., Acharya, V. N., Almeida, A. F., Channakeshavamurthy, A., Ballal, H. S., P, G., Issacs, R., Jasuja, S., Kirpalani, A. L., Kher, V., Modi, G. K., Nainan, G., Prakash, J., Rana, D. S., Sreedhara, R., . . . Rajapurkar, M. M. (2013). Epidemiology and risk factors of chronic kidney disease in India – results from the SEEK (Screening and Early Evaluation of Kidney Disease) study. *BMC Nephrology*, 14(1). https://doi.org/10.1186/1471-2369-14-114
29. Sontrop, J. M., Dixon, S. N., Garg, A. X., Buendia-Jimenez, I., Dohein, O., Huang, S. H. S., & Clark, W. F. (2013). Association between Water Intake, Chronic Kidney Disease, and Cardiovascular Disease: A Cross-Sectional Analysis of NHANES Data. *American Journal of Nephrology*, 37(5), 434–442. https://doi.org/10.1159/000350377
30. Stump, C. S. (2011). Physical Activity in the Prevention of Chronic Kidney Disease. *Cardiorenal Medicine*, 1(3), 164–173. https://doi.org/10.1159/000329929

31. Tatapudi, R. R., Rentala, S., Gullipalli, P., Komarraju, A. L., Singh, A. K., Tatapudi, V. S., Goru, K. B., Bhimarasetty, D. M., & Narni, H. (2019). High Prevalence of CKD of Unknown Etiology in Uddanam, India. *Kidney International Reports*, 4(3), 380–389. https://doi.org/10.1016/j.ekir.2018.10.006
32. Wang, V., Vilme, H., Maciejewski, M. L., & Boulware, L. E. (2016). The Economic Burden of Chronic Kidney Disease and End-Stage Renal Disease. *Seminars in Nephrology*, 36(4), 319–330. https://doi.org/10.1016/j.semnephrol.2016.05.008