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Chronic kidney disease and its associated risk factors: A case control study

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Abstract
Chronic kidney disease (CKD) has become a global health issue and with the rising cost of nephrology care, there is need to understand the risk factors which predispose to its development and the consequent means of mitigating its development and progression. This study on "chronic kidney disease and its associated risk factors: a case-control study" was carried out on adults within the area under study to ascertain the association between CKD and some risk factors of interest to the researcher. This study involved 109 cases who were matched by age and sex with 109 controls, all drawn from the same population. The results show that hypertension (p = 0.030; 95%CI =0.321, 0.944), obesity (p = 0.014; 95%CI =1.175, 4.303), alcohol use (p = 0.021, 95%CI = 0.055, 0.790), and awareness of the disease were found to have statistically significant association with CKD whereas diabetes (p=0.6695, 95% CI= 0.373, 1.929), smoking (p = 0.596; 95%CI =0.325, 7.069), age, and sex did not show statistically significant association with CKD in this study. Having a relationship with a person diagnosed of CKD was the only variable that had a statistically significant association with respect to family history (p = 0.011, χ^2 = 9.00). However, the odd for CKD was lower in the non-diabetic subjects by 15% (16% in the adjusted analysis). The same was observed with sex where the odd for CKD was found to be about 1.3 times (OR=1.282) higher in females than in males. For the fact that the risk factors of CKD have been found to vary between countries and climes, it is expedient that they be studied in smaller geographic locations in order to detect the risk factors a particular area is prone to. This therefore underscores the need for increased emphasis on screening and managing the modifiable risk factors early enough so as to forestall the development and progression of the disease, seeing that the course of the disease is irreversible in nature.

Keywords: association, case-control study, chronic kidney disease, risk factors

1. Introduction
Chronic kidney disease (CKD), a non-communicable disease which is characterized by the gradual loss of kidney function over a period of time has been adjudged the 12th highest cause of death and the 17th cause of disability worldwide [1]. The disease is progressive and irreversible in nature with the earliest stages being asymptomatic. The implication then is that a significant amount of kidney function is lost before the disease is detected [2, 3]. In 2002, [4] defined CKD as "the presence of kidney damage or decreased level of kidney function maintained for three months or more, irrespective of the primary diagnosis or cause". Many risk factors have been established to have association with CKD even though these vary between climes and studies. Most of the implicated risk factors are chronic disease conditions such as hypertension, diabetes, glomerulonephritis, systemic lupus erythematosus, inherited polycystic kidney disease and sickle cell nephropathy among others. Obesity, dyslipidemia, age, family history of the disease, awareness of the disease and lifestyle factors such as smoking and alcohol use have also been implicated [5, 6, 7, 8, 9, 10]. According to [11], the adequate knowledge of the risk factors connected to the development of chronic kidney disease, and more importantly the risks that compete with regards to the two major outcomes namely end-stage renal-disease (ESRD) and death, is fundamental to the prevention of the disease. Thus, while primary prevention tends to focus on the healthy population, secondary and tertiary prevention aim at the apparently diseased and diseased groups [12, 13].

Early diagnosis of CKD and prompt management of the predisposing conditions coupled with intentional lifestyle changes will go a long way to limit the progression of the kidney disease. In fact, there is reliable evidence to show that "treatment can prevent or delay the progression of CKD; reduce or prevent the development of complications; and reduce the risk of cardiovascular disease" [14]. The earlier the intervention, the greater the effect of the intervention. Important aspects of nephrology care include the halting of disease progression, treatment of pathologic presentations of CKD and prompt planning for renal replacement therapy if the occasion arises.

However, as noted by [15] the prevalence of CKD has been given as an estimate between the range of 10 and 20 percent. In Nigeria, the prevalence obtained from studies carried out in different parts of the country is between 1.6 and 30 percent [16, 17, 7, 6].

Using a case-control study, it could be determined if an association exists between CKD and the risk factors of interest in this particular population and maybe by extension the general population. Where evidence of association is found between CKD and specific risk factors, those at risk of developing CKD will be easily identified and measures will thereby be put in place to checkmate the development and progression of the disease.

2. Materials and Methods
2.1 Study Design
This is a population-based case-control study which entailed the examination of the subjects to ascertain the existence of

kidney damage (presence of albuminuria) and/or reduction in kidney function (evidenced by reduced glomerular rate). Those with evidence of kidney damage and/or reduction in kidney function were categorized as cases whereas those with normal kidneys/functions who do not fall into the category earlier described were designated as non-cases (controls). The participants who were diagnosed with CKD were further divided into stages 1,2,3,4 and 5 depending on the degree of albuminuria/proteinuria and estimated glomerular filtration rate.

2.2 Study Population
This study was carried out in four out of the nine Local Government Areas of Owerri Senatorial Zone of Imo-State Nigeria. The subjects were adults 18 years and above who were selected using multi-stage sampling technique from various households. Simple random sampling and systematic random sampling were employed at different stages of the selection. Written informed consent was also obtained from the subjects.

2.3 Selection of Cases and Controls
The cases were determined using the results from urinalysis where proteinuria was sought for together with the serum creatinine values which were used in the calculation of the estimated glomerular filtration rate (eGFR) using the modification of diet in renal disease (MDRD) equation which is given as: $eGFR=175 \times Cr^{-1.154} \times Age^{-0.203} \times 0.742$ (if female) x 1.212 (if black). On the other hand, the controls used for this study were selected from the non-cases identified after the afore-mentioned laboratory procedures. A total of 109 cases were obtained from the four Local Government Areas after the whole analysis and these cases were matched with 109 controls by age and sex.

2.4 Stage Classification of Chronic Kidney Disease

Stage	Description	GFR (ml/min/1.73m^2)
1	Kidney damage with normal or ↑GFR	>90
2	Kidney damage with mild ↓ GFR	60-89
3	Moderate ↓ GFR	30-59
4	Severe ↓ GFR	15-29
5	Kidney failure with or without dialysis	<15 (D+/D-)

2.5 Variables of Interest
The risk factors of interest in this study were diabetes, hypertension, obesity, smoking, alcohol use, age, sex, family history and awareness of the disease.

2.6 Administration of Questionnaires
The well-structured questionnaires were also used to elicit information on the socio-demographic characteristics of the subjects together with other relevant information such as family history, hypertension status, diabetes status, smoking and alcohol use among others.

2.7 Data Analysis
Data analysis was performed on IBM-SPSS statistical package version 21 and EPI-INFO 7. Descriptive methods were used to describe some data summary characteristics; hence data are presented on charts and frequency distributions which were used to express the percentage of the distribution. To determine the association between CKD and the metabolic syndromes (hypertension, diabetes, obesity) as well as between CKD and lifestyle factors (smoking, alcohol use) logistic regression was performed in two phases. The same logistic regression analysis was used to ascertain the association between age and sex. A Chi-Square test was used to test for association between CKD and family history and as well as the association between CKD and its awareness level. The odds ratio was also calculated as a measure of the strength of the association between each of the exposures (the risk factors of interest) and the outcome which in this case is CKD. Confidence interval (CI) at 95% level was also calculated for each odds ratio. Probability value (P) was used to identify the significant risk factors at 5% level hence P less than 5% (or 95% CI not containing one) was considered significant for the risk factors.

3. Results
The prevalence of CKD as was obtained from this study is given as 14.5%. Then, among the 109 CKD cases studied, the largest number of cases 44 (40.3%) were in the stage 3b, followed by those in stage 1 at 31 (28.4%) and those in stage 2 at 18 (16.5%). Those in stage 3a of the disease were 11 (9.2%) while those in stage 4 were 6 (5.5%) (Figure 1). No case was recorded in stage 5 of the disease.

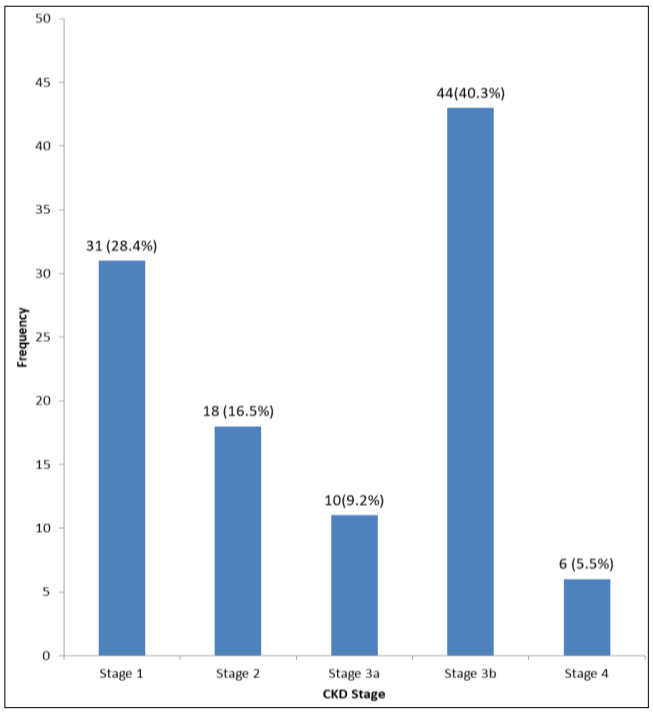

Fig 1: Distribution of CKD Cases by Stage Classification

The outcome of the test of association between chronic kidney disease and the studied risk factors is as presented in Table 1. Hypertension was found to be statistically a significant risk factor of CKD in this study, both in the adjusted ($p < 0.009$; AOR = 0.457; 95%CI =0.254, 0.821) and unadjusted ($p = 0.030$; 95%CI =0.321, 0.944) analysis. Among the normotensive subjects, the odds for CKD was found to be 45% (i.e. 1-0.55) significantly lower compared to that of the hypertensive. On the other hand, diabetes was not found to be statistically a significant risk factor of CKD (p=0.6695, 95% CI= 0.373, 1.929), even though the odd for CKD was lower in the non-diabetic subjects by 15% (16%

in the adjusted). Using the logistic regression analysis, it can be deduced that there is a statistically significant association between obesity and CKD (p = 0.014; 95%CI =1.175, 4.303). Among the obese subjects, the adjusted odds for CKD was found to be over 2.2 times significantly higher when compared to that of the non-obese subjects. Using the logistic regression analysis also, alcohol use was found to be statistically significant at 5% level in the adjusted analysis (p = 0.021, 95%CI = 0.055, 0.790). The adjusted odd ratio (AOR) of 0.209 is a clear indication that the non-alcohol consuming subjects have lower odds of CKD of about 79% compared to that of the alcohol consuming subjects. The odd was found to be significantly lower for those who take alcohol several times per week (p = 0.026, 95% CI = 0.016, 0.770) and those who consume it once per week (p = 0.017, 95%CI = 0.025, 0.697), compared with those that take alcohol daily by 89% and 87% respectively. The number of years the participants have been taking alcohol was not found to be statistically significant.

Cigarette smoking was not found to be statistically a significant risk factor of CKD in this study (p = 0.596; 95%CI =0.325, 7.069). The same was observed with age, sex, and family history. However, the odd for CKD appears to be more on the 60-69 years of age (1.01 times) and on the ≥ 80 years of age (1.24 times), compared to that of the reference age group (<40 years old) while the odds for CKD was found to be up to 1.3 times (OR =1.282) higher in females than in males in this study. From the results available from this study, using the Chi-Square test, none of the variables representing family history of CKD was found to be significantly associated with the disease in this study statistically except family relationship with the person diagnosed of CKD (p = 0.011, χ^2 = 9.00), nevertheless, the odds for CKD was found to be 52% (i.e. 1 -0.48%) lower for the subjects who do not have family members diagnosed of CKD than for those with family members diagnosed of the disease (OR =0.48) (Table 2). With respect to awareness of CKD, statistically significant sources of awareness include radio (p = 0.0003, χ^2 = 13.26) and television (p = 0.0073, χ^2 = 7.20) (Table 2).

Table 1: Association between Chronic Kidney Disease and Some Risk Factors

Risk Factors	Cases N (%)	Controls N (%)	Total N (%)	P – Value	Odds Ratio	CI- 95% Lower Upper
Hypertension						
Yes	57(52.3)	48 (44.0)	105 (48.0)	0.030	0.550	0.321 0.944
No	52 (47.7)	61 (56.0)	113 (52.0)			
Diabetes						
Yes	14 (12.8)	12 (11.1)	26 (11.9)	0.6695	0.848	0.373 1.929
No	95 (87.2)	97 (88.9)	192 (88.1)			
Obesity						
Non-Obese	85 (78.0)	73 (67.0)	158 (72.5)	0.014	2.249	1.175 4.303
Obese	24 (22.0)	36 (33.0)	60 (27.5)			
Smoking						
Yes	3 (2.8)	6 (5.5)	9 (4.1)	0.596	1.517	0.325 7.069
No	106 (97.2)	103 (94.5)	209 (95.9)			
Alcohol Use						
Yes	32 (29.4)	36 (33.0)	68 (31.2)	0.021	0.209	0.055 0.790
No	77 (70.6)	73 (67.0)	150 (68.8)			
Age (Years)						
<40	7 (6.4)	6 (5.5)	13 (6.0)	Reference		
40-49	15 (13.8)	15 (13.8)	30 (13.8)	0.817	0.857	0.233 3.159
50-59	23 (21.1)	24 (22.0)	47 (21.6)	0.754	0.821	0.240 2.814
60-69	30 (27.5)	24 (22.0)	54 (24.8)	0.911	1.071	0.318 3.612
70-79	21 (19.3)	30 (27.5)	51 (23.4)	0.414	0.600	0.176 2.042
≥80	13 (11.9)	10 (9.2)	23 (10.6)	0.762	1.238	0.311 4.934
Sex						
Male	36 (33.0)	31 (28.4)	67 (30.7)	0.401	1.282	0.718 2.290
Female	73 (67.0)	78 (71.6)	151 (69.3)			

Table 2: Association between Chronic Kidney Disease, family history and awareness of CKD

Risk Factor	Cases N (%)	Controls N (%)	Total N (%)	P -Value	Odds Ratio	χ^2
Family History						
Yes	3 (2.8)	6 (5.5)	9 (4.1)	0.307	0.48	1.043
No	106 (97.2)	103 (94.5)	209 (95.9)			
Awareness of CKD						
Yes	38 (34.9)	31 (28.4)	69 (31.7)	0.308	1.34	1.04
No	71 (65.1)	78 (71.6)	149 (68.3)			

4. Discussion

The prevalence of CKD and distribution of the various stages as was obtained in this study tends to agree with the estimated global prevalence of between 11-13% with the majority being in stage 3 [18]. More so, according to the systematic review conducted by [19] on studies carried out on CKD in Nigeria, the observed prevalence of CKD in this study was close to what was obtained in some of the studies they reviewed particularly those where the eGFR was calculated using the MDRD formula. Some other studies like the one conducted by [6] in Nigeria however show a higher prevalence of CKD. The participants in stages 1 and 2 make up about 45% of the entire cases, a figure which is quite significant.

From the available results, hypertension came out as a significant risk factor for CKD in both the adjusted and unadjusted analysis. A great percentage of the participants in this present study were hypertensive (about 48.0%), and among them are those who even though they are hypertensive, do not take medications to control the condition. It was also observed that many people do not check their blood pressure as often as they ought, more especially with increasing age. Thus, there is need to manage those with hypertension promptly and appropriately to minimize the progression of the disease and thereby a consequent decline in kidney functions.

Furthermore, the obtained results suggest that being hypertensive is enough to cause development of chronic kidney disease irrespective of other variables, although proper management can mitigate the further progression of the disease. Even though diabetes was not found to be statistically a significant risk factor of CKD, the odd of CKD is decreased in non-diabetic subjects when compared to the diabetic subjects. The prevalence of diabetes among the studied subjects was given as 11.9%. From the available information as generated from this study, a significant number of the cases were not aware that they have developed hypertension while some of them were also not aware that they have diabetes. The same is applicable also to the significant number of the control subjects who did not know that they had hypertension and diabetes prior to this study. It is also frightening to note that those who fall within this category presented with very high blood pressure and blood sugar levels.

As was also observed from the results, a positive coefficient was obtained between obesity and CKD implying that obesity is a significant risk factor for CKD. The adjusted odds for CKD was observed to be over 2.2 times significantly higher among the obese when compared with that of the subjects who were non-obese. The prevalence of obesity in this study was found to be 27.5%.

The prevalence of hypertension, diabetes mellitus, and obesity was found to be 28.9%, 4.2% and 30% respectively in the work carried out by [20]. They also found age, female gender, BMI and dyslipidaemia to be predictive of CKD in their study. The findings of the study conducted by [21] are quite close to what was found in this study with respect to the recorded prevalence of hypertension, diabetes, and obesity among the population they studied. In addition, they found an association between CKD and hypertension, diabetes mellitus, heart disease, myocardial infarction and waist to hip ratio, while no association was found between CKD and BMI.

As was obtained in this study, the association between cigarette smoking and CKD was not statistically significant and the prevalence of cigarette smoking among the study participants was also not that high. This statistically insignificant association observed in this study may also be explained by the small number of the subjects who smoke, both among the cases and controls. A greater proportion of the study population was observed to use alcohol, and in the adjusted analysis, alcohol intake was found to be statistically significant at 5% level. The adjusted odd ratio of 0.209 clearly indicates that the odds of CKD is lower (about 79%) among non-alcohol consuming subjects when compared to that of the alcohol consuming subjects, and the odd was also found to be significantly lower for those who take alcohol several times per week and those who consume it once per week when compared with those who take alcohol on daily basis. One can therefore deduce that daily alcohol consumption is a very dangerous practice that increases the risk of developing CKD. This calls for intensive campaign for lifestyle changes among the populace seeing that alcohol use as a lifestyle factor can predispose one to CKD.

Although the association between age and CKD was also not statistically significant in this study, the odds for CKD seem to be more on the 60-69 years of age and on the ≥ 80 years of age when compared to that of the reference age group (<40 years old). This result of association does not seem to tally with what is believed conventionally about CKD and age, but none the less this observed difference could be because of the fewer number of younger people selected for this study.

As was observed in this study [22], also had more female participants than males in their study. In the community-based study conducted by [23] in Uganda, a greater percentage of the participants were also females. Although previous studies such as those of [21] and [24] suggest that being female is a significant risk factor for CKD, the result from this study reveals that even though the odd for CKD is higher in females than in males, being a female was not found to be statistically significant with regards to its association with CKD.

Just like in the association between age and CKD, the association between CKD and family history was not statistically significant, even though the odds for CKD was higher among the subjects with family history of CKD than those who did not have relations with CKD. This statistical insignificance might be attributable to the small number of subjects in the study who had relations with a history of CKD.

The awareness of the disease among the population studied was not as high as expected by the researcher, even though its association with CKD was found to be statistically significant. This is worrisome, because the implication is that where there is little or no knowledge of the risk factors as well as the preventive measures among the people, there is an increased tendency for people to become victims of these issues they know little or nothing about. This poor level of awareness of the participants in this study is quite unlike the study population used by [21] whose level of awareness of the disease was adjudged very high by the researchers and they attributed the decline in ESRD observed among populations of such characteristics to be as a result of their increased level of awareness. It then implies that the more aware a person is of a disease with respect to its risk factors, prevention and control strategies among others, the likelihood it is for the person to be protected from the disease. The place of the mass media particularly those of the electronic media cannot be overemphasized, looking at how significant they were with respect to awareness of CKD.

Although, some of these studied risk factors of CKD have been established as having significant association with CKD, the fact remains that most times differing variables such as the characteristics of a particular target population, the setting, mode of selection of participants and research design among others affect the final results obtained. For instance, in the study carried out by [23], risk factors such as diabetes, smoking and alcohol intake were not found to be significantly associated with CKD, whereas the same were

found as independent predictors of CKD in the study carried out by [24].

5. Conclusion

This study has been able to x-ray the relationship between CKD and the risk factors studied. It also gave insight to the prevalence of CKD and the distribution of the various stages of the disease among the cases. There is therefore need to step up preventive and control measures in order to curtail the development and progression of these implicated risk factors particularly the modifiable risk factors. It is also expedient that more elaborate campaigns are mounted to enlighten the general population about the inherent danger of living with uncontrolled chronic disease conditions such as hypertension.

Conflict of interest: None declared.

6. References

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