

Association between Body Mass Index as A Measure of Excess Weight and Glomerular filtration rate among Healthy Nigerian Population

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Conflict-of-interest statement: The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

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Received: August 17, 2018

Revised: October 5, 2018

Accepted: October 8, 2018

Published online: October 23, 2018

ABSTRACT

BACKGROUND: There is an increasing interest in the relationship between excess weight and the occurrence of kidney disease. Reports from studies examining the significance of body mass index (BMI) as a risk factor for development of CKD have been largely controversial. Such studies are sparse among the indigenous Nigerian population.

OBJECTIVE: We examined the relationship between increased weight and renal function among participants during a public medical screening programme.

METHOD: This is a cross sectional study involving 659 participants during a public medical screening programme. The Participants were categorized into two groups; those with eGFR ≥ 60 and < 60 mL/min/1.73m². BMI was calculated and classified using the WHO criteria. Correlation was performed with Pearson's correlation test. Logistic regression was used to examine the association between BMI and CKD after adjusting for potential cofounders.

RESULTS: The mean age of the participants was 39.11 ± 15.18 years. About one third were overweight while 18.2% had BMI 30.0 kg/m² or greater. There was a significant difference in the mean eGFR among person with normal weight compared with obese individuals and a negative association between eGFR and BMI (-0.339 , $p = 0.000$). Logistic regression showed that higher BMI remained independently associated with CKD (OR 1.218, 95% CI 1.084-1.368 $p = 0.000$) after adjusting for potential cofounders.

CONCLUSION: These findings showed that excess weight has a significant association with glomerular filtration rate and should be considered an important risk factor for CKD. Keeping a healthy range BMI may contribute to the prevention of chronic kidney disease.

Keywords: Body Mass Index; Estimated glomerular filtration rate; Obesity.

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Dada SA, Raimi TH, Aremu AO. Association between Body Mass Index as A Measure of Excess Weight and Glomerular Filtration Rate among Healthy Nigerian Population. Journal of Nephrology Research 2018; 4(1): 153-158 Available from: URL: <http://www.ghrnet.org/index.php/jnr/article/view/2400>

INTRODUCTION

Obesity is a well-recognized risk factor for diabetes and hypertension worldwide^[1]. The risk for chronic kidney disease is notably increased in individual with these conditions^[2-4]. In a national survey of adults in the United States, the age-adjusted prevalence of obesity in 2013-

2014 was 35.0% among men and 40.4% among women^[5].

Overweight and obesity are on the rise in Africa with imminent epidemic. Current estimate shows that as much as 20-50% of urban populations in Africa are classified as either overweight or obese^[6,7].

With the increasing incidence of hypertension and diabetes worldwide and other non-communicable diseases, the number of individuals with chronic kidney disease (CKD) will likely continue to rise. Studies have shown that obesity measured by body mass index (BMI) is associated with the development of CKD^[8-10].

Krammer *et al.*^[11] were able to demonstrate a higher incidence of CKD associated with increased BMI. In contrast, other studies reported that anthropometric indexes of abdominal obesity, waist circumference (WC), and waist-to-hip ratio (WHR) are more sensitive predictors of CKD^[12,13].

The exact mechanisms whereby obesity may cause or worsen CKD remain unclear. It has been postulated that the presence of obesity solely may not explain the characteristic renal damage seen in overweight and obese individuals but may involve a combination of hemodynamic, metabolic, and inflammatory changes^[1].

Obesity is frequently accompanied by hypertension, dyslipidaemia^[11], metabolic syndrome, insulin resistance^[11,14] and oxidative stress^[15]. These factors may collectively influence the risk for CKD in overweight and obese individuals.

Guidelines for the detection and assessment of kidney disease was developed by the National Kidney Foundation (NKF)^[16]. CKD was defined as the presence of kidney damage and/or a glomerular filtration rate (GFR) < 60 ml/min/1.73m² body surface area for ≥ 3 months. Kidney damage may be indicated by increased urine albumin excretion, histological changes in the kidney or abnormalities in the urine sediment and/or imaging tests. The guidelines also described further the stages of CKD according to the GFR as follows; Stages 1 and 2 are defined as normal (≥ 90 ml/min/1.73m²) or mildly decreased (60-89 ml/min/1.73m²) GFR respectively, in the presence of other markers of kidney damage. Stages 3-5 are classified as a GFR < 60 ml/min/1.73m² regardless of other markers of kidney damage. Stage 5 includes patients with kidney failure or GFR < 15 ml/min/1.73m².

To the best of our knowledge, less attention has been paid to the effect of excess weight and development of CKD especially in this part of the world.

We examined the relationship between increased weight (*i.e.*, BMI) and renal function evaluated by the estimated glomerular filtration rate (eGFR) in adults who participated in a community-based screening conducted in Ado Ekiti, South West Nigeria.

METHODS

Sampling

Data used for this study was obtained from the screening conducted in Ado Ekiti, South West Nigeria in a survey for indices of kidney damage in all the six geopolitical zones of the country. The study methods and materials have been previously published^[17].

Briefly, Ado Ekiti is the headquarter which also doubles as the capital of Ekiti State. It is an urban settlement with a current estimated population of about 424,340^[18]. The major occupations of the residents are trading, semi-skilled work and public service. Carbohydrate is the major component of their food intake while there is a recent upsurge in the adoption of western diets. The participants were mobilized through radio and television jingles as well as handbill. The announcement was made in English and local dialects.

After consent was obtained, participants' biodata was documented and they were instructed to proceed to sample collection points where

blood and urine specimens were taken for laboratory analysis.

Clinical and laboratory measurements

The weight was measured using a standardized bathroom scale, while the height was measured with a Stadiometer. The body weight and height were assessed to the nearest 0.1 kg and 1 cm respectively with all subjects standing without shoes or heavy outer garments. The body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters using the WHO Criteria^[19]. BMI (in kg/m²) status was categorized as follows: Underweight; < 18.5 ; normal; 18.5-24.9; overweight; 25-29.9; obese; ≥ 30 .

The blood pressure was measured from the left upper arm using Accusson's mercury sphygmomanometer. Elevated blood pressure was defined by a systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg^[20]. Hypertension was taken to be present if the participant reports prior diagnosis at a hospital and being on prescribed antihypertensive medication.

Five millilitres of blood was taken into heparinized sample bottles for evaluation of urea, creatinine, cholesterol, and triglyceride levels. Serum creatinine levels were calibrated to an assay traceable to isotope-dilution mass spectrometry.

Blood chemistries analysis were performed on the centrifuged samples with Mindray chemistry analyzer (BS-200 China) at a reference laboratory. The re-expressed MDRD Study equation with the standardized serum creatinine assay was used to determine the glomerular filtration. $GFR = 30849 \times \text{standardized serum creatinine}^{-1.154} \times \text{age}^{-0.203} \times 0.742$ (if female) $\times 1.21$ (if black) [mL/min/1.73m²]^[21,22].

The Participants were categorized into two groups: those with an eGFR ≥ 60 and < 60 mL/min/1.73m².

Random blood glucose (in mmol/l) was done on site using AccucheK® glucometer (Roche diagnostics). Diabetes was taken to be present if the participant reports prior diagnosis at a hospital and being on prescribed glucose lowering medication.

Urinalysis was performed using Combi-9® urinalysis strips. Menstruating women were instructed not to provide urine samples. Ethical clearance was obtained from the Ekiti State University Teaching Hospital

Statistical analysis

Statistical analysis was performed using SPSS® version 20 (SPSS Inc., Chicago). Data were stratified by BMI categories (normal weight, overweight and obese). Numerical data were presented as mean \pm SD or median as appropriate while categorical data were expressed in percentages. Correlation was performed with the Pearson's correlation test. Multiple logistic regression analyses were used to estimate odds ratio (OR) and 95% confidence intervals (CI) for the association between eGFR and BMI while adjusting for potential cofounders such as age, sex, blood pressure and history of smoking. A *P* value < 0.05 was considered significant.

RESULTS

Subject characteristics

Among the 863 participants, 204 individuals were excluded due to missing or incomplete data. Of the remaining 659 subjects, 33.1% were found to be hypertensive while 48 (7.3%) had diabetes mellitus. The mean age of the participants was 39.11 ± 15.18 years with a range of 18-85 years. Three hundred and seventy-nine (57.5%) were female. The characteristics of all participants are shown in Table 1 according to BMI categories. Three hundred and seventy-nine (48.1%) had normal weight, about one third (33.7%) were overweight

while 18.2% had BMI 30.0 kg/m² or greater.

There is no significant difference in the mean value of total cholesterol among the obese and the non-obese, $p = 0.279$.

There is a significant difference in the mean value of eGFR among person with normal weight compared with obese individuals, $p = 0.001$. Older participants were more likely to be obese compared to younger participants Table 2.

We found a weak but statistically significant negative association between eGFR and BMI ($-0.339, p = 0.000$) Figure 1.

Multivariate analysis adjustments for factors significantly associated with low eGFR

Logistic regression was performed to assess the relationship between BMI and eGFR ≤ 60 ml/min/1.73m². Higher BMI remained

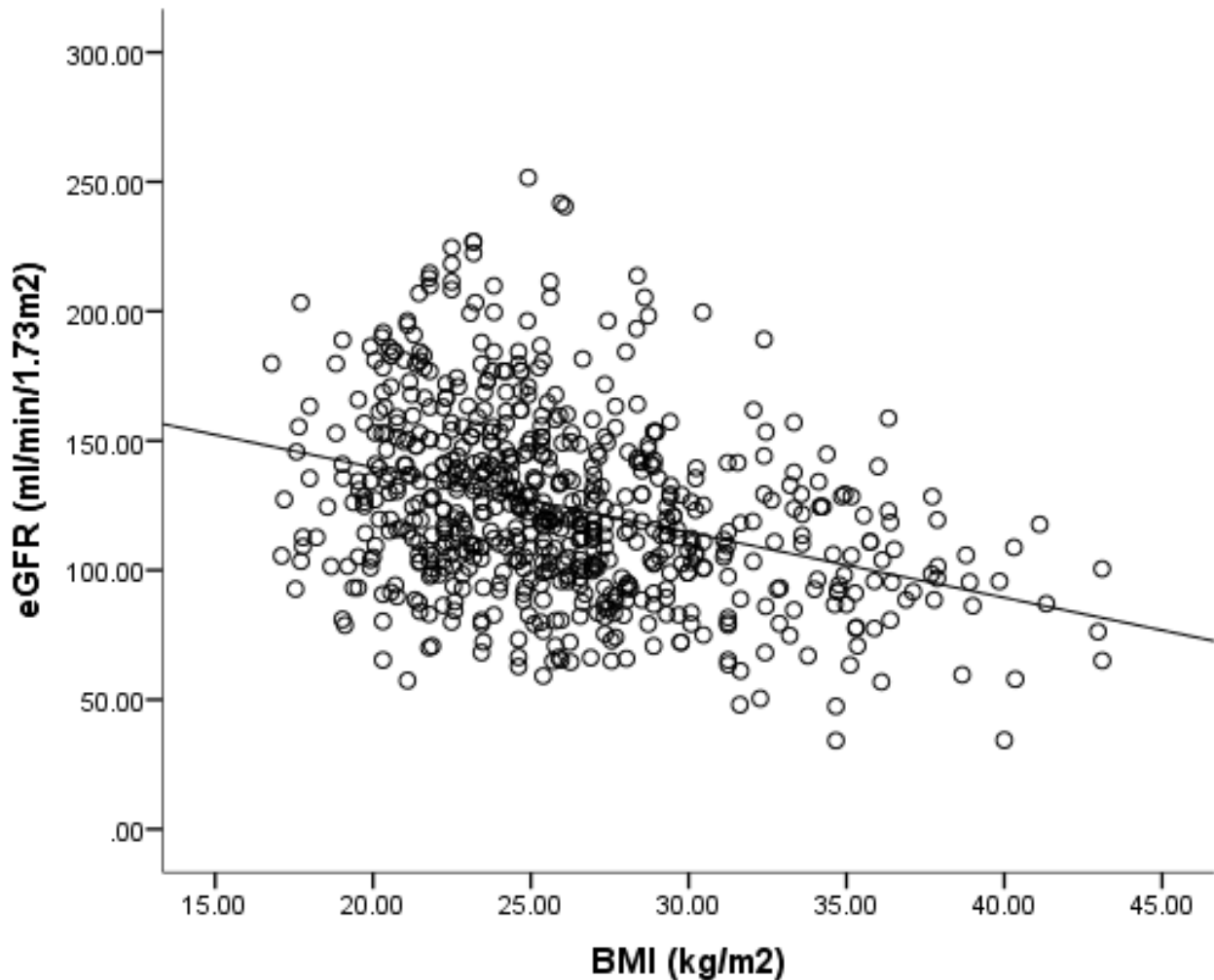


Figure 1 Relationship between eGFR and BMI.

Table 1 Participants characteristic across BMI strata

Characteristics	BMI < 25 kg/m ²	BMI 25-30 kg/m ²	BMI > 30 kg/m ²	P Trend
No. of participants	317	222	120	
Age (yr)	35.13 (33.47-36.78)	42.28 (40.30-44.27)	43.77 (41.36-46.17)	0.001
Women (N, %)	143 (44.5)	137 (61.4)	99 (86.1)	0.000
Smoking (%)	3.8	0.5	0.8	0.017
Weight (kg)	60.71 (8.10)	71.49 (7.27)	85.53 (9.37)	0.000
Height (m ²)	1.65 (0.85)	1.62 (0.70)	1.58 (0.65)	0.000
BMI (kg/m ²)	22.2 (1.89)	27.17 (1.40)	34.20 (3.14)	0.000
eGFR (mL/min/1.73m ²)	135.87 (35.56)	119.70 (33.03)	103 (29.01)	0.000
Blood pressure (mmHg):				
Systolic	125.16 (19.13)	133.21 (23.62)	133.44 (22.68)	0.001
Diastolic	76.65 (11.13)	79.46 (12.78)	80.75 (12.25)	0.000
FBS (mmol/L)	5.29 (1.39)	5.76 (2.62)	6.00 (2.19)	0.002
Creatinine (μmol/L)	70.51 (14.00)	72.78 (14.34)	78.82 (22.09)	0.000
Cholesterol (mmol/L)	4.07 (1.30)	4.14 (1.24)	4.24 (1.27)	0.447

eGFR: estimated glomerular filtration; BMI: Body mass index; FBS: fasting blood sugar.

independently associated with CKD (OR 1.264, 95% CI 1.133-1.410 $p = 0.000$). The association was maintained after adjustment for potential confounders such as sex, hypertension, age and total cholesterol. (OR 1.218, 95% CI 1.084-1.368 $p = 0.001$) Table 3.

DISCUSSION

Chronic kidney disease (CKD) is a common and growing public health problem worldwide^[23,24].

With the increasing incidence of hypertension and diabetes worldwide and other non-communicable diseases, the number of individuals with CKD will likely continue to rise.

In our study, we found a weak but statistically significant negative association between eGFR and BMI, suggesting that those with a high BMI had the kidney dysfunction. Other studies examining this relationship have shown inconsistent results. Hobbs *et al*^[25] demonstrated lack of association between BMI and GFR however, they reported a statistically significant difference in GFR across BMI strata on multivariate analysis. A prospective cohort study among the whites by Foster *et al*^[26] reported a positive correlation between BMI and GFR which completely disappeared after adjustment for other confounders such as diabetes and hypertension.

In the Physician's Health Study involving 11,104 healthy men, Gelber *et al*^[27] reported an association between BMI and increased risk of CKD. He observed that 1,377 participants (12.4%) had a GFR of < 60 mL/min/ 1.73 m² after an average 14-year follow-up.

In a study lending support to the concept that BMI may be an independent risk factor for CKD, Kramer *et al*^[11] in his analysis of data from the Hypertension Detection and Follow-Up Program (HDFP), found that both baseline overweight (OR, 1.21; 95% CI, 1.05 -1.41) and obesity (OR, 1.40; 95% CI, 1.20-1.63) were associated with increased odds of incident CKD at year 5 after adjusting for confounders. Similar results were observed after exclusion of participants with baseline diabetes mellitus, with both overweight (OR, 1.22; 95% CI, 1.05-1.43) and obesity (OR, 1.38; 95% CI, 1.17-1.63) remaining significantly associated with incident CKD.

After adjusting for potential cofounders such as age, sex, race, smoking status, serum cholesterol level among others, higher BMI was found to be a risk factor for ESRD according to Hsu *et al*^[8]. They also observed a graded trend in the Odds of CKD as the BMI increased. The harmful effect of obesity on the kidneys also include other complications such as renal cancers and nephrolithiasis. Bhaskaran *et al* estimated that more than 10% of kidney cancers are attributable to overweight and obesity. He concluded that a 5 kg/m² increase in BMI was associated with 25% higher risk of kidney cancers^[28].

Genetic susceptibility, sleep apnea syndrome^[29] and reduced nephron number^[4] have been proposed to play roles in the development of obesity-related secondary focal segmental glomerulosclerosis (FSGS).

Another postulate to explain obesity mediated kidney disease involves adipose tissue facilitated up-regulated release of inflammatory cytokines^[30,31], insulin resistance^[15] and leptin^[32]. This inflammatory damage is probably mediated through the resident fibroblast in the kidney. It has been postulated that resident fibroblasts activate NF- κ B signaling and produce pro-inflammatory cytokines and chemokines thus promoting inflammation^[33].

Ramos *et al* showed that elevated BMI and body fat percentage independently predict oxidative stress and inflammation in moderate to severe CKD^[15].

Table 2 Clinical characteristic among Obese and non-obese participants.

Characteristics	Obese	Non Obese	P value
Age (mean year \pm SD)	43.77 \pm 13.33	38.08 \pm 15.39	0.000
Blood Pressure (mm/Hg)			
Systolic	133.44 \pm 22.68	128.47 \pm 21.44	0.024
Diastolic	80.75 \pm 12.25	77.22 \pm 11.97	0.004
Fasting blood Sugar (mmol/l)	5.90 \pm 2.16	5.50 \pm 2.01	0.049
Total cholesterol (mmol/l)	4.24 \pm 1.27	4.10 \pm 1.34	0.279
Serum creatinine (μ mol/l)	78.83 \pm 22.09	71.44 \pm 14.17	0.001
eGFR (ml/min/1.73m ²)	103.06 \pm 29.01	129 \pm 21 \pm 35.00	0.000

Table 3 Result of BMI and Multivariable-Adjusted ORs and 95% CIs for CKD.

	Variables	B	95% CI	P value
Model 1	BMI	1.264	1.133-1.410	0.000
Model 2	BMI	1.218	1.084-1.368	0.001
	Sex	4.923	0.411-59.006	0.208
	Age	1.106	1.048-1.167	0.000
	Total cholesterol	0.926	0.493-1.735	0.808
	Systolic BP	0.989	0.910-1.054	0.579

BP: blood pressure.

Excess adipose tissue can also lead to activation of the sympathetic nervous, renin-angiotensin systems, hyperfiltration, and other pathophysiological perturbation leading to development of hypertension with consequent damage to the kidneys^[34,35].

Though we did not find any significant difference in the cholesterol level among the obese and the non-obese participants in this study, nonetheless, hyperlipidemia is also considered to be a risk factor for developing CKD^[11,36].

In exploring the risk factors affecting the incidence of chronic kidney disease among the Japanese general population, Yamagata *et al* found that hyperlipidemia and low HDL-C were independent risk factors for proteinuria which is a strong predictor for renal dysfunction^[37].

Excessive accumulation of body fat has been found to initiate cascade of cellular events and progressive inflammatory mediated obesity-associated chronic diseases^[38].

CONCLUSIONS

Our findings confirmed that excess weight has a significant association with glomerular filtration rate and should be considered as an important risk factor for CKD. Keeping a healthy range BMI may contribute to the prevention of chronic kidney disease.

Such preventive strategies aimed at reducing obesity-related chronic kidney disease must include adoption of healthy nutrition, routine physical exercise and regular screening.

Limitations: we have some limitations in this study, this includes single assessment of eGFR and absent data on albuminuria.

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Peer Reviewer: Monchai Siribamrungwong