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PREVALENCE OF PREDIABETES AND THE ASSOCIATED RISK OF KIDNEY DISEASE IN APPARENTLY HEALTHY SUBJECTS IN NNEWI, ANAMBRA STATE, NIGERIA

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ABSTRACT

This study was designed to investigate the prevalence of prediabetes and the associated risk of kidney disease in Nnewi, Nigeria. A total of 277 apparently healthy subjects (73males and 204 females) who were willing to participate were recruited. Anthropometric indices and blood pressure were measured using standard methods while the demographic data and dietary pattern of subjects were obtained using a well-structured questionnaire. 5mls of blood was collected from eligible subjects (20 prediabetes and 20 non prediabetes) and dispensed in fluoride oxalate and plain containers for glucose, creatinine (Cr), Urea(Ur), Na+, K+, Cl-, and HCO3- estimation respectively using standard methods. The result showed a prevalence of 7.2% prediabetes in the population. BMI was significantly higher in prediabetes than the control groups (39.4±5.8 vs 29±4.4kg/m2; P>0.05). Again, significant increases in the prediabetic values of FBG (117.54±16.84 vs 83±16.84mg/dl; P>0.05) than the control group were observed. The SBP (128± 11.26 vs 120±2.2mmHg; P>0.05) and DBP (92±4.43 vs 60±5.3mmHg; P>0.05) was also higher in prediabetic groups. Interestingly, result showed no significant difference between the renal parameters in prediabetes and non prediabetes (p>0.05). The study therefore, suggests that the major determinant for predabetes in the study population may be hypertension and obesity whereas kidney function was not impaired.

Contribution/Originality: This study documents the Prevalence of Prediabetes and the associated risk of kidney disease in apparently healthy individuals in Nnewi, Anambra State, Nigeria.

1. INTRODUCTION

Diabetes is a very complex medical issue. World Health Organisation defines Diabetes mellitus as a "chronic disease caused by inherited and or acquired deficiency in production of insulin by the pancreas, or by the ineffectiveness of the insulin produced. Such a deficiency results in increased concentrations of glucose in the blood, which in turn damage many of the body's systems, in particular the blood vessels and nerves"[1]. Prediabetes refers to the intermediate metabolic states between normal and diabetic glucose homeostasis, it is a risk state that defines a high chance of developing diabetes. Prediabetes is an intermediate state of hyperglycemia with glycemic parameter above normal but below the diabetes threshold [2]. When diagnosed with prediabetes, one is at a higher risk for developing diabetes in the future. Prediabetes is characterized by impaired fasting plasma glucose, 5.6-6.9mmol/L (100-125mg/dl) and impaired glucose tolerance 2 hours after 75g glucose load, 7.8-11.0mmol/L (140-198mg/dl) [3]. These conditions are known as impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) respectively. PD subjects do not manifest any symptoms of impaired glucose metabolism but are at increased risk of developing renal complications and type 2 Diabetes mellitus (Dm) [4]. Prediabetes

may not result in type 2 diabetes if lifestyle changes are made. Therefore, screening for PD in apparently healthy individual will help to reduced risk of developing type 2 DM. Prediabetes is the medical stage in which not all of the symptoms required to label a person as diabetic are present, but blood sugar is abnormally high. As the prevalence and incidence of Dm increase rapidly worldwide, so will the prevalence and incidence of PD increase, since the latter is a natural history of the former [5]. In the current issue of Diabetes Care, Bullard, et al. [6] review secular trends in U.S, Prediabetes prevalence using National Health and Nutrition Examination Surveys(NHANES) data from 1999 to 2010. The authors conclude that prediabetes is increasing in prevalence and that demographic subgroups may benefit from targeted diabetes prevention efforts. Research study suggests that high levels of glucose could be affecting kidneys even prior to diabetes diagnoses [7]. Kidney failure is a serious condition when kidneys fail to eliminate the body's waste and is the final stage of chronic kidney failure. Diabetic kidney damage may start much earlier than previously thought according to new study published in the National kidney foundation's American journal of kidney diseases. Researchers discovered that fasting glucose levels consistent with prediabetes are independent risk factors for hyperfiltration in the kidneys and the presence of albumin in the urine which are all indicators of kidney disease. They also show that the pathological process of kidney injury caused by elevated blood glucose levels starts in prediabetes ,well before the onset of diabetes [7]. There are many causes of kidney failure which include high blood pressure, glomerulonephritis, urologic diseases, or cystic disease. Among those causes, diabetes is the most common cause of kidney failure accounting for almost 44% of new patient cases, Even with tight controls over blood glucose, patients with diabetes can still progress to kidney failure [7]. However, recent research shows that for the kidneys problems may begin to occur in prediabetic stage, long before a patient is actually diagnosed with diabetes. The study conducted at the university hospital of North Norway in Toronto, found that evidence of kidney damage that is typically associated with diabetes actually starts when blood sugar levels are consistent with prediabetes [7]. Screening for albuminuria and measurement of serum creatinine, urea and Electrolytes are currently recommended by the American Diabetes Association for the diagnoses of either diabetes or prediabetes and annually thereafter (standard of medical care in diabetes,2009). There is no doubt that chronic kidney disease is a common complication of diabetes mellitus [8] and is associated with important adverse outcomes, such as cardiovascular disease and mortality [9]. Factors that are associated with higher risk for Chronic Kidney Disease (CKD) include hypertension, diabetes and obesity. Diabetes is a major cause of CKD, and prediabetes accompanies increased prevalence of CKD as well. For the National Health and Nutrition Examination Survey (NHANES) study, Plantinga, et al. [10] reported that 39.6% of people with diagnosed diabetes and 41.7% with undiagonised diabetes had CKD,17.7% with prediabetes and 16% without any kind of diabetes had CKD. The reason for more cases of CKD in prediabetes has not been determined. Mascrovascular disease may not be the cause. For, et al. [11] from the Framingham Heart study observed a stronger association between other cardiovascular risk factors and CKD observed in patients with prediabetes is due to macrovascular disease, especially hypertension and not in microvascular disease. Recent studies also showed that prediabetes is the leading cause of kidney failure accounting for 44% of new cases of kidney failure [7]. Some data indicated that lifestyle interventions for prediabetes can return individuals for normoglyceamia Perreault, et al. [12] and Schellenberg and Dryden [13]. The aim of this study is to evaluate the prevalence of prediabetes and its associated risk of kidney diseases in adult males and females in Nnewi, Anambra state, Nigeria. Hence, the outcome of this study may help to identify individuals with prediabetes which will offer them the opportunity to modify their risk prior to development of significant sequelae such as kidney diseases and cardiovascular diseases and also to report trends in prediabetes for individuals without previously diagnosed to be diabetics.

2. MATERIALS AND METHODS

2.1. Study Area

Nnamdi Azikiwe University, Okofia-Otolo, Nnewi campus comprises the College of Health Sciences having the faculties of Basic Medical Sciences, Health Sciences and Technology and Medicine. It is located in the suburb of Nnewi - a popular town in Anambra State Nigeria. The environment is poorly developed and lacking basic amenities such as housing, road, communication, electricity and potable water compared to campuses located in urban areas.

2.2. Study Design

On the day preceding each data collection, subjects were informed to eat dinner not later than 10 p.m. and be present on each morning of the study, which was to commence by 7 a.m., without eating any food or drink. Questionnaires were distributed to obtain the subject's demographics, knowledge, family history of diabetes, physical activity levels, and general dietary habits. Blood pressure and anthropometric parameters were obtained using standard procedures [14-16]. 5mls of blood was collected from eligible subjects. 2mls of blood was dispensed in fluoride oxalate and 3mls into plain tubes for plasma glucose and other biochemical parameters respectively. Plasma Fasting blood sugar (FBS) and 2-hours post prandral (2THPP)glucose as well as renal functions (Creatinine,Urea) and Electrolytes Na+, K+, Cl-, HCO3-) were analyzed using standard methods described by Bergmeyer and Bernt [17]; Carl, et al. [18]; Taylor [19] *and Ion Selective Electrode* respectively While the glomerular filtration rate (GFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) 2009 formula as described by Inker and Levey [20].

2.3. Inclusion Criteria and Exclusion Criteria:

Apparently healthy male and female subjects aged 45 years and above were recruited for the study. Subjects younger than 45years, pregnant, known diabetic, those with cardiovascular disease and heart failure as well as those on drugs were excluded from this study.

2.4. Ethical Consideration

Ethical approval was obtained from the Faculty of Health Sciences and Technology ethical committee, Nnamdi Azikiwe University, Nnewi campus, Anambra State, Nigeria for sample collection.

2.5. Statistical Analysis

Statistical package for social science (SPSS) version 20 was employed in the analysis of the result and the data obtained for different renal parameters and arthropometric parameters between different groups using student's independent t-test and pearson correlation. Level of significance was set at $P<0.05$.

3. RESULTS

The demographics of the study population were illustrated in (table1). Of all the 277 participant ,73 (26.4%) were males while 204 (73.6%) were females (Table 2). This research study showed (7.2%) prevalence as seen in 20 subjects of the 277 study population; out of which 3 (15%) are males and 17 (85%) are females. The results of the anthropometric assessment of the participants (Table 2) showed that there was significant increase in the mean values in Height(Ht),Weight(89.05 ±13.6) and also Body mass index (BMI)(39.44±5.86) of the prediabetes subjects when compared with the controls group's weight(72±5511.19) and BMI (29.19±4.41) respectively. The mean level FBG (Table 3) of the prediabetic group was 117.54±16.84mg/dl while the mean for THPP was (150.93±24.71mg/dl) indicating that the FBG and THPP in prediabetic individuals were significantly higher than the control group.

Table 4 showed the mean values of the renal parameters in prediabetes and the control subjects. There were no significant differences in the renal parameters of the prediabetics and control individuals ($p>0.05$). Table 5 shows the mean values of the renal parameters of the male and female prediabetes. There was no significant difference between male and female renal parameters ($p> 0.05$). Table 6 showed the result of systolic blood pressure (SBP) and diastolic blood pressure(DBP) in prediabetes and control. The result showed that there was a significant difference in systolic blood pressure (SBP) and diastolic blood pressure (DBP) ($p<0.05$) between prediabetes and control subjects. Table 7 showed no association between the renal parameters (urea, creatinine, Na, K, CL and HCO_3) and prediabetes parameter(THPP and FBG). Table 8 showed a significant inverse correlation between Creatinine and GFR ($p<0.05$)

Table-1. Demographics of the participants

Variables	Number	No of prediabetes	Percentage (%)
Total population	277	20	7.2
Male	73	3	4.1
Female	204	17	8.3

Source: Apparently Healthy Subjects in Nnewi, Anambra State, Nigeria.

Table-2. The Arthropometric parameters of prediabetes and control(mean±SD)

Variables	Pre-diabetes N=20	Control N=20	t-value	p-value
Age(yrs)	50.95±11.27	49.30±9.96	0.491	0.627
Ht(m)	149.80±5.16	156.15±6.62	-3.384	0.002*
Wt(kg)	89.05±13.6	72.55±11.19	4.188	0.000*
HWC(inch)	1.05±0.11	1.03±0.19	0.428	0.671
BMI(kg/m^2)	39.44±5.86	29.19±4.41	6.392	0.000*

P-value is significant at<0.05

Table-3. Fasting blood glucose and two hours post prandral of prediabetes and control (Mean±SD)

Variables	Pre-diabetes N=20	Control N=20	t-value	p-value
FBS(mg/l)	117.54±16.84	83±16.84	9.22	0.000*
THPP(mg/l	150.95±24.71	80±24.71	7.25	0.000*

Source: Apparently Healthy Subjects in Nnewi, Anambra State, Nigeria; * P-value is significant at<0.05.

Table-4. Renal parameters in prediabetes and control subjects (Mean ± SD).

Renal parameters	Prediabetes	Control	t-value	p-value
Urea (mmol/l)	3.06±1.30	2.86±0.92	0.645	0.523
Creat (mmol/l)	95.35±20.74	91.15±27.77	-0.232	0.818
Na (mmol/l)	1.39±3.98	1.40±4.54	38.00	0.380
Cl (mmol/l)	99.75±3.91	1.01±4.33	38.00	0.258
K(mmol/l)	4.62±1.15	4.76±1.26	37.66	0.726
BCo(mmol/l)	22.45±1.19	22.40±0.94	36.05	0.884
GFR(mmol/l)	77.60±23.94	90.10±23.60	37.99	0.105

* P-value is significant at<0.05.

Table-5. Renal parameters in male and female(Mean±SD)

Renal parameters	Male	Female	t-value	p-value
Urea(mmol/l)	2.89±0.68	2.98±1.04	-0.233	0.817
Creat(mmol/l)	95.63±25.53	96.41±25.29	-0.081	0.936
Na(mmol/l)	1.41±3.11	1.39±4.46	1.155	0.255
Cl(mmol/l)	1.02±3.74	1.00±4.21	1.149	0.258
K(mmol/l)	4.74±0.97	4.68±1.26	0.118	0.907
BCo(mmol/l)	22.38±0.92	22.44±1.11	-0.147	0.884
GFR	91.88±29.31	81.84±22.98	1.045	0.302

*P value is significant at<0.05.

Tabl-6. The Systolic and Diastolic blood pressure among the prediabetes and control (Mean±SD).

Variables	Population N=20	Control N=20	t-value	p-value
SBP(mm/Hg)	128.±11.26	120±2.2	8.50	0.000*
DBP(mm/Hg)	92±4.43	60±5.3	3.99	0.000*

*P value is significant at<0.05.

Table-7. Association of renal parameters with prediabetes

Variables	r-value	p-value
Urea vsFBS	0.061	0.799
Urea vs THPP	-0.233	0.323
Creat vs FBS	-0.375	0.103
Creat vs THPP	0.125	0.601
Na vs FBS	0.023	0.922
Na vs THPP	-0.115	0.628
Cl vs FBS	-0.096	0.686
Cl vs 2HPP	-0.126	0.598
K vs FBS	0.128	0.591
BCO vsFBS	0.105	0.659
BCO vs 2HPP	0.158	0.064
GFR vs FBS	0.380	0.098
GFR vs 2HPP	0.064	0.788

*P value is significant at<0.05.

Table-4.8. Association of anthropometric parameters and renal parameters with prediabetics. (N=20)

Variables	r-value	p-value
Creat vs GFR	-0.838**	0.000
Na vs Cl	0.932**	0.000

*P value is significant at<0.05.

4. DISCUSSION

This study investigated the prevalence of prediabetes and its associated risk of kidney disease in apparently healthy individuals in Nnewi, Anambra state, Nigeria. This population (apparently healthy individuals) were specifically studied because prediabetes is not a disease condition but it can predispose one to diabetes mellitus if lifestyle is not modified. This study found that the prevalence of prediabetes in the study population was generally decreased. Few studies in different geopolitical zones of Nigeria identified high prevelance rates of prediabetes in study population. The first reported prediabetes condition in Nigeria was in 1998 [21]. They found a prevalence of 2.2% in a group of urban adults in Nigeria. Subsequently, Nwatu, et al. [22] reported a prevalence of 21.5% in an urban community in Enugu state and Ogbu and Nebo [23] who reported the 25% prevalence of prediabetes among hypertensive in Enugu. The gradual increase overtime may be attributed to increase in change of life style and dietary modifications. However, in this present study, the subjects were most market people with relatively low income, compounded by the economic downturn of the country. Their daily activity also involves frequently regular physical activities like trekking, farming, etc, which reduces their risk of been prediabetic.

In this study however, most of the prediabetic subjects had high abdominal obesity, which is in consonance with the studies that showed that the reason for the high prevalence of prediabetes is overweight and obesity, which may be due to the presence of insulin resistance and toxicity to beta cells due to the high level of free fatty acids in obese individuals [24, 25]. In this study, SBP and DBP were higher in prediabetes compared with the control individual, which is an indication that they are predisposed to hypertension or prehypertension. This agrees with findings of Gupta and Gupta [26] who showed a significant difference in the same parameter in prediabetics. The possible mechanism is that the activity of angiotensin II is increased in the circulatory system of patients with hypertension. Angiotensin II activates rennin- angiotensin aldosterone system (RAAS) and affects the function of the pancreatic islets, resulting in islet fibrosis and reduced synthesis of insulin and ultimately leading to insulin resistance [26]. The study conducted by Song, et al. [27] also showed that increased age, obesity and high fat diet are predisposing factors for prediabetes. They proposed that screening, early intervention in people with a family history of diabetes and obesity was crucial to reduce the risk of diabetes. Previous studies have reported that overweight and obesity were the main factors contributing to insulin resistance and insulin resistance was the basis of prediabetes and diabetes.

This study also found out that, there was no significant difference between renal parameters in prediabetes compared with control subjects. The non significant changes in glomerula filtration rate was attributed to the use of estimated glomerular filtration rate (eGFR) rather than measured (mGFR) [7]. There was however, a significant inverse correlation between creatinine and GFR which is in conformity with the findings by Manjunath, et al. [28] that showed that it might be due to effects of age, sex, and to a lesser extent race, on creatinine production. Melson, et al. [7] also showed an increase in the same parameter in adult prediabetes, this suggests that an increase in glomerular filtration rate , may probably be due to increased renal blood flow and changes in fluid distribution.

5. CONCLUSION

In conclusion, from this study, the prevalence of prediabetes was generally decreased in the study population and also there was no significant association between prediabetes and kidney disease. Although there was a very high significant values of Body mass index, systolic and diastolic blood pressure in prediabetics, suggesting that the major determinant for prediabetes, in this urban community may be hypertension and obesity.

6. RECOMMENDATIONS

Since the prevalence is low in this study population, it is therefore recommended that constant re-evaluation of the incidence and prevalence is done, preferably a country wide study in order to establish the true picture of the incidence and prevalence in Nigeria. Also kidney function should be monitored in subjects with prediabetes or prehypertension . Hyperglycemia and high blood pressure should be treated as early as possible to prevent the development of kidney damage. Since the findings from this study suggest that the major determinant for prediabetes in this urban community may be hypertension, it is likely that measures such as campaigns for reduction in salt intake may be beneficial.

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