- **Title of paper** – One in Ten Apparently Healthy Nigerian Adults has Concurrent Prediabetes and Prehypertension – Findings from a Community-based Survey.

Short running title – Prediabetes & prehypertension in Nigeria

ABSTRACT

Aim – To determine the prevalence of concurrent prediabetes and prehypertension among apparently healthy Nigerian adults in a rural Nigerian community.

Study design: The study was cross-sectional.

Place and Duration of Study: Ihuokpara, Nkanu East Local Government Area Enugu State Nigeria, May 2013.

Methodology - Eight hundred and twenty four (538 females and 286 males)consenting adult residents of Ihuokpara, a rural community in Enugu State of Nigeria, were recruited for the study through a cross-sectional, stratified, convenient sampling technique. A structured questionnaire assessed subject's socio-demographic data, detailed anthropometric indices and blood pressure using standard protocols. Subject's fasting plasma samples in addition to 2-hour post 75-gram-glucose-load plasma samples were assessed for glucose levels.

Results - The mean age of the participants was 51.1±16.2 years; females constituted 65.3% of the subjects and 46.3% of the study population had no formal education. Concurrent prediabetes and prehypertension was prevalent at 10.4% with no significant gender bias (*P* =.13). Older age, physical inactivity and impaired glucose tolerance were significant predictors of concurrent prediabetes and prehypertension (*P* =.007, .003 and .006 respectively) with older age and physical inactivity emerging as consistent significant predictors, after logistic regression models.

Conclusion - There was a high prevalence of concurrent prediabetes and prehypertension among adults in this rural Nigerian community.

Key words

Concurrent, Prediabetes, Prehypertension, Prevalence, Rural, Nigeria.

1. INTRODUCTION

Prediabetes, characterized by plasma glucose values between normal and diabetic range (1) and marginally raised blood pressure levels known as prehypertension (2) independently, pave the way for adverse cardiovascular events. When present simultaneously in an individual, their combined effect may then translate to an ultra-short; ultra-fast freeway to untoward cardiovascular outcomes (3). The burden of concurrent prediabetes and prehypertension (pre-DM/HTN) and associated cardio-metabolic risk in apparently healthy, Nigerian adults is yet to be documented.

Cardiovascular disease (CVD) is a major cause of morbidity and mortality in both developed and developing countries and imposes a major strain on the economy and health care manpower which typically, is sparse in low and middle income countries such as Nigeria

Prediabetes is a well-documented risk factor for CVD, riding on the back of insulin resistance (IR) with resultant endothelial dysfunction, pro-coagulant state and inflammation. (4) It comprises impaired fasting glucose (IFG); impaired glucose tolerance (IGT) or both. (5)

The American Diabetes Association (ADA) defines IFG as fasting plasma glucose concentrations ranging from 5.6mmol/L (100mg/dl) to 6.9mmol/L (125mg/dl) and IGT as plasma glucose concentrations from 7.8mmol/L (140mg/dl) to 11.1mmol/L (199mg/dl), 2 hours after a 75g glucose load; during an oral glucose tolerance test (OGTT). (6)

The International Diabetes Federation (IDF) has projected sub-Saharan Africa as the region to record the most increases in prediabetes and diabetes prevalence in the near future. (1)

Nigeria alone accounts for one-sixth of the total population of the region (7) and has a clear lead among other African countries, in the estimated projection for future diabetes prevalence and number of people currently living with diabetes. (1)

A recent community-based study in Nigeria revealed a prevalence rate for prediabetes (combined IFG and IGT) at 21.5% (8), using the World Health Organization (WHO) criteria. Left untreated, up to 70% of individuals with prediabetes may eventually progress to frank diabetes if followed up for up to five years or more. (1, 19)

Hypertension is another important risk factor for CVD, with minimal elevations of blood pressure shown to be associated with adverse cardiovascular outcomes (10, 11) prompting the Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-7) to create a new category called prehypertension. The JNC-7 defined prehypertension as systolic blood pressure (SBP) ranging from 120-139mmHg, and/or diastolic blood pressure (DBP) from 80-89mmHg. (2)

A recent meta-analysis of pooled data of 561,664 participants from 17 prospective cohort studies showed unequivocally that prehypertension also increased the risk of coronary heart disease. (11) The National Health and Nutrition Examination Survey (NHANES) 1999-2000 reported a worldwide prevalence of prehypertension at 31% and prehypertension was noted more in men than in women. (12) A study of two ethnic populations in Africa done in northern Nigeria revealed a high prevalence for prehypertension at 58.7%. (13) Another population-based study revealed a sustained increase in prevalence of point prehypertension among Nigerian adolescents from 15.1% among 13 year olds to 37.2% among 18 year olds. (14)

Individuals with prehypertension are at increased risk of progressing to true hypertension if measures to halt or reverse it are not instituted (10). Therefore, as prediabetes and prehypertension individually result in clear-cut cardiovascular risks; co-existing pre-DM/HTN in the same subject may synergistically, lead to even more severe adverse cardio-metabolic outcomes. (3)

The black race is a strong risk factor for both prediabetes and prehypertension (15, 16) and in spite of the above daunting figures from Nigeria, there is no available data or literature on the prevalence of concurrent prediabetes and prehypertension in any Nigerian population. The prevalence of coexisting prehypertension and prediabetes among healthy American adults was 11.2±0.6% while among Chinese adults, the prevalence was 11.0% (17, 18)

Hence, this study aimed to ascertain the prevalence of concurrent pre-DM/HTN among apparently healthy Nigerian adults. Data obtained will help to form policy towards preventive measures as prediabetes and prehypertension are early 'warning' phases in the natural history of diabetes and hypertension respectively; two very common chronic and burdensome diseases in Nigeria.

2. METHODOLOGY

2.1 STUDY AREA

The study was carried out in the nine villages that make up Ihuokpara, a rural community in Nkanu east local government area of Enugu state, southeast Nigeria in March 2013. The community is approximately 35 to 40 kilometers from Enugu, the state capital. The community lacks basic social amenities like access roads, clean water supply and electricity and has an estimated population of 12,000 people. (19)

2.2 STUDY DESIGN

The study was cross-sectional in nature.

2.3 STUDY POPULATION

Included were adult residents aged 18 years and above except those who refused consent while pregnant women and nursing mothers were excluded from the study.

2.4 ETHICAL CONSIDERATIONS

The health research and ethics committee of the University of Nigeria Teaching Hospital approved the study and protocols conform to the revised provisions of the Declaration of Helsinki 1964.

2.5 SAMPLE SIZE

Using the prevalence rate of 34.6% for prediabetes in Seychelles (20), sample size was calculated as 348 using Fisher's formula for a cross-sectional study. However, to allow for design effects, 824 subjects eventually completed the study.

2.6 SAMPLE TECHNIQUE

After an extensive awareness for the study had been created by the study investigators, with the assistance of the paramount ruler and the local town criers, a multistage stratified cluster sampling technique was employed using the extended families and clans as clusters to recruit qualified participants from each village at each given day until all the villages had been sampled.

2.7 DATA COLLECTION

Subjects presented on each morning of the study, after an overnight fast of 10 hours. Subjects then had a pre-recruitment briefing by the study investigators and assistants, and verbal informed consent obtained from each participant.

A structured questionnaire, modeled after the WHO-STEPs questionnaire was administered to the subjects and their demographic information was obtained. Knowledge of common symptoms and family history of diabetes and hypertension were assessed including their physical activity levels and general dietary habits.

Blood pressure (BP), weight, height and waist circumference (WC) of subjects were measured using standard protocols. (21)

Height was measured to the nearest 0.1m with a stadiometre and without subject wearing any footwear or headgear. Weight was obtained using a standard pre-calibrated weighing scale on a flat surface with subject wearing minimal clothing and was recorded to the nearest 0.5kg. Waist circumference was measured with a non-stretchable tape, midpoint between the last rib and the superior iliac crest, along the mid axillary line and was recorded to the nearest 0.5cm.

Subject's BP was obtained using Accoson mercury sphygmomanometers, with the mean of two readings taken 5 minutes apart recorded.

Plasma glucose was estimated from a fingertip pinprick blood sample, using pre-standardized Accu-Check Active® glucose metres and corresponding test strips. The test strips had been pre-calibrated by the manufacturer, Roche Diagnostics GmBH, Germany, © 2011 using the hexokinase method so that results were comparable to venous plasma glucose concentrations as recommended by the International Federation of Clinical Chemistry and Laboratory Medicine.

The fasting plasma glucose (FPG) value of each subject was assessed after which an oral glucose tolerance test (OGTT) was administered using 75g of anhydrous glucose powder, dissolved in 250mls of clean cold water. A subsequent finger-prick blood sample obtained two hours after the 75g glucose load was assessed for glucose levels.

2.8 DEFINITIONS OF STUDY CRITERIA

An FPG value from 5.6 to 6.9mmol/L (100-125mg/dl), with a 2-hour plasma glucose of <7.8mmol/L (<140mg/dl) represents IFG – ADA criteria. (6)

A 2HPP plasma glucose value of >7.8 - <11.0mmol/L (140-199mg/dl), with FPG of <5.6mmol/L (<100mg/dl) represents IGT – ADA criteria. (6)

Hypertension represents an SBP ≥140mmHg and/or DBP ≥90mmHg – WHO/International Society of Hypertension guidelines. (22)

An SBP of 120-139 mmHg and/or a DBP of 80-89 mmHg defined prehypertension – JNC-7 guidelines. (2)

Obesity was defined using the WHO criteria. Cut-off values for BMI were: Overweight (25.0 – 29.99kg/m^2) and Obesity (≥30kg/m^2) (23)

Central obesity was based on the International Diabetes Federation (IDF) guidelines where WC of ≥94cm for males and ≥ 80cm for females were considered raised. (24)

2.9 STATISTICAL ANALYSIS

The data obtained was recorded in Microsoft excel-2007, analyzed using SPSS software Version 20.0 (SPSS Inc. Chicago Illinois, USA) and summarized as means and standard deviations. Continuous variables were reported as percentages; differences between categorical variables were analyzed with chi square or Fishers exact test while differences between continuous variables were analyzed using the Student's T test. All tests for significance were two-tailed with $P = .05$.

3. RESULTS AND DISCUSSION

3.1 SOCIO-DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF SUBJECTS

Out of the 824 adults studied, 34.7% were males while 65.3% were females. The mean age of the subjects was 51.1 ± 16.2 years and the males were older than the females with mean ages of 53.3 ± 16.0 years and 49.9 ± 16.2 years respectively ($P = .004$).

Farming was the predominant occupation of the subjects as 73% of the population, were subsistent farmers. Other demographic and clinical characteristics are as shown in Table 1.

Table 1. Socio-demographic and clinical characteristics of the study population

Parameter	Male	Female	Total	*P*
Age group (years)				
18-39 (%)	90(10.9)	188(22.8)	278(33.7)	0.005*
40-64 (%)	110(13.3)	242(29.4)	352(42.7)	
>65 (%)	86(10.4)	108(13.1)	194(23.5)	

Physical activity				
Active (%)	280(34.0)	512(62.1)	792(96.1)	0.05
Inactive (%)	6(0.7)	26(3.2)	32(3.9)	
Educational status				
None (%)	102(12.4)	280(34.0)	382(46.3)	<0.001*
Primary (%)	132(16.0)	204(24.8)	336(40.8)	
Secondary and above (%)	52(6.4)	54(6.5)	106(12.9)	
BMI (kg/m^2)	23.2 ± 3.7	23.6 ± 3.9	23.5 ± 3.9	0.95
SBP (mmHg)	138.0 ± 27.1	136.0 ± 27.8	136.7 ± 27.6	0.33
DBP (mmHg)	84.6 ± 15.8	81.1 ± 13.9	82.3 ± 14.7	0.001*
FPG (mg/dl)	95.3 ± 14.9	95.2 ± 17.0	95.2 ± 16.3	0.95
2HPPG (mg/dl)	119.7 ± 14.9	122.8 ± 37.1	121.7 ± 35.2	0.24

*Denotes significant values. Abbreviations: BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; FPG = fasting plasma glucose; 2HPPG = 2-hour post-prandial glucose.

3.2 PREHYPERTENSION

The mean SBP of the subjects was 136.7 ± 27.6mmHg while the mean DBP was 82.3 ± 14.7mmHg. The prevalence of prehypertension was 34.8% and was present in 39.5% of the males and in 32.3% of the females. The characteristics of the subjects with prehypertension were compared with normal subjects after excluding those with hypertension. This is as shown below in Table 2.

166 **Table 2. Characteristics of subjects with prehypertension compared with normal subjects**

Parameter	Prehypertension present (N=287)	Prehypertension absent (N=166)	Total (N=453)	*P*
Gender				
Male (%)	113(73.9)	40(26.1)	153(33.8)	0.004*
Female (%)	174(58.0)	126(42.0)	300(66.2)	
Age (years)	49.2 ± 17.3	43.4 ± 17.1	47.1 ± 17.4	0.001*
Physical activity				
Active (%)	275(95.8)	162(97.8)	437(96.5)	0.33
Inactive (%)	12(4.2)	4(2.2)	16(3.5)	
BMI (kg/m^2)	23.3 ± 3.4	22.8 ± 3.3	23.1 ± 3.4	0.21
SBP (mmHg)	124.2 ± 7.3	107.5 ± 6.6	118.1 ± 10.8	<0.001*
DBP (mmHg)	75.9 ± 6.0	68.6 ± 5.1	73.2 ± 6.7	<0.001*
FPG (mg/dl)	94.2 ± 12.9	91.6 ± 14.6	93.3 ± 13.6	0.05
2HPPG (mg/dl)	123.7 ± 35.1	116.2 ± 26.1	120.9 ± 32.3	0.02*

167 *Denotes significant values. Abbreviations: BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; FPG = fasting plasma

168 glucose; 2HPPG = 2-hour post-prandial glucose.

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3.3 PREDIABETES

The mean FPG of the subjects was 94.8±16.4 mg/dl, while the mean 2HPP glucose level after an OGTT was 122.7±39.7 mg/dl.

Prediabetes (either/both IFG and IGT) was present in 276 (33.5%). The prevalence of IFG alone (27.2%) was however higher than that of IGT alone (15%). The prevalence of prediabetes was not significantly different between males and females (11.4% and 22.1% respectively, p = 0.95). In Table 3, characteristics of subjects with prediabetes were compared with those who had neither prediabetes nor diabetes.

Table 3. Characteristics of subjects with prediabetes compared with normal subjects

Parameter	**Prediabetes Present N = 276 (%)**	**Prediabetes Absent N = 495 (%)**	**Total N = 771 (%)**	***P***
Gender				
Male	94(34.1)	174(35.2)	268(34.8)	0.76
Female	182(65.9)	321(64.8)	503(65.2)	
Physical activity				
Inactive (%)	10(3.6)	20(4.0)	30(3.9)	0.77
Active (%)	266(96.4)	475(96.0)	741(96.1)	
Age (years)	52.4 ± 15.9	49.9 ± 16.5	50.8 ± 16.3	0.05
BMI (kg/m^2)	23.8 ± 4.2	23.3 ± 3.6	23.5 ± 3.8	0.07
FPG (mg/dl)	102.7 ± 10.6	87.7 ± 8.4	93.1 ± 11.7	<0.001*

2HPPG (mg/dl)	129.4 ± 25.6	109.3 ± 21.9	116.5 ± 25.2	<0.001*
SBP (mmHg)	138.7 ± 27.4	135.8 ± 27.9	136.8 ± 27.8	0.17
DBP (mmHg)	83.7 ± 15.3	81.8 ± 14.5	82.5 ± 14.8	0.09

*Denotes significant values. Abbreviations: BMI = body mass index; FPG = fasting plasma glucose; 2HPPG = 2-hour post-prandial glucose; SBP = systolic blood pressure; DBP = diastolic blood pressure.

3.4 PREDIABETES AND PREHYPERTENSION

Eighty-nine subjects (10.4%) had both preDM/HTN, out of which 32 (34.4%) were males while 61 (65.6%) were females. Their other characteristics are as shown in Table 4.

Table 4. Characteristics of subjects with both prehypertension and prediabetes

PARAMETER	**MALES**	**FEMALES**	**TOTAL**	***P***
	N=32 (%)	**N=61 (%)**	**N=93 (%)**	
Age (years)	56.8 ± 19.0	45.6 1± 7.2	49.2 ± 18.5	0.007*
Physical activity				
Active (%)	25(28.1)	60(67.4)	85(95.5)	0.003*
Inactive (%)	4(4.5)	0(0)	4(4.5)	
BMI (kg/m^2)	23.2 2.8	23.1 3.5	23.1 3.2	0.87
SBP (mmHg)	126.9 ± 5.1	125.5 ± 5.6	125.9 ± 5.4	0.26
DBP (mmHg)	77.9 ± 7.1	75.4 ± 6.5	76.2 ± 6.8	0.11
FPG (mg/dl)	100.0 ± 10.4	103.8 ± 9.2	102.6 ± 9.7	0.09
2HPP (mg/dl)	140.1 ± 34.6	122.5 ± 23.3	128.2 ± 28.5	0.006*

*Denotes significant values. Abbreviations: BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; FPG = fasting plasma glucose; 2HPPG = 2-hour post-prandial glucose.

When the subjects with both pre-DM/HTN were compared to those with neither characteristic (normal subjects), those with concurrent pre-DM/HTN were found to be significantly older with a mean age of 50 years versus 40 years for normal subjects (p = <0.001). In addition, subjects with both conditions had significantly higher WC and BMI values compared to normal subjects (p = 0.03 and p = 0.015 respectively).However, no significant gender differences were found in the subjects who had both conditions when compared with normal subjects.

Logistic regression analyses were done to determine predictors of prehypertension, prediabetes and concurrent pre-DM/HTN. The results are as shown in Table 5 below.

Table 5. Binary Logistic regression to determine predictors of prehypertension, prediabetes and concurrent pre-DM/HTM

PREDICTORS OF PREHYPERTENSION					
Variable	**B coefficient**	**SE**	**Exp (B)**	***P***	**95% CI**
Sex	-0.649	0.218	0.523	0.003*	0.341 - 0.801
Age (>45 yrs)	-0.588	0.201	0.556	0.003*	0.375 – 0.824
BMI (>25 kg/m^2)	-0.532	0.248	0.588	0.032*	0.361 – 0.955
Prediabetes	-0.264	0.222	0.768	0.235	0.497 – 1.187
PREDICTORS OF PREDIABETES					
Sex	0.234	0.224	1.263	0.297	0.814 – 1.960

Age (>45yrs)	0.652	0.213	0.521	0.002*	0.343 – 0.792
BMI (>25 kg/m^2)	0.348	0.254	1.416	0.171	0.861 – 2.330
Prehypertension	-0.223	0.220	0.800	0.311	0.520 – 1.232
PREDICTORS OF CONCURRENT PRE-DM/HTN					
Sex	-0.534	0.353	0.586	0.130	0.294 – 1.170
Age (>45yrs)	-0.878	0.309	0.416	<0.004*	0.227 – 0.761
Physically inactive	-1.421	0.624	0.242	0.023*	0.071 – 0.821
BMI (> 25 kg/m^2)	0.120	0.384	1.127	0.906	0.531 – 2.391
WC (cm)	-1.250	0.682	0.286	0.067	0.075 – 1.091

*Denotes significant values. Abbreviations: BMI = body mass index; WC = waist circumference. B coefficient = beta coefficient; SE = standard error; Exp (B) = exponent value of beta coefficient; CI = confidence interval.

In this rural community in south-east Nigeria, with a very high level of physical activity among the subjects, one in every ten adults was found to have concurrent pre-DM/HTN, two significant factors driving the non-communicable diseases (NCDs') epidemic in Nigeria. The rising epidemic of NCDs in Nigeria reported by Maiyaki and Garbati in their study has been attributed to globalization with attendant changes in lifestyle and dietary habits. (25) The WHO estimates that NCDs account for a quarter of total deaths in all ages and among both sexes in Nigeria, with CVD and diabetes together, accounting for 9% of these deaths. (26) Our results also reflect findings from studies among Chinese and American adults (17, 18) though these populations may actually have higher values than reported in their respective studies, as subjects with IGT were not identified using the OGTT.

The low socio-economic status noted in this population, evidenced by low exposure to formal education; lack of basic social amenities and an exposure to chronic stressors with majority of the subjects being subsistent farmers, may have contributed to the high prevalence of the two conditions. Low socio-economic status has been shown to be associated with adverse cardio-metabolic indices. (27) In addition, Winkleby et al also found that higher CVD risk was associated with lower socioeconomic status, with lower educational levels emerging as the strongest predictor of CVD risk among the parameters they assessed. (28)

There was no significant gender-based difference in prevalence of concurrent pre-DM/HTN contrary to findings in the Chinese and American studies where significant male preponderance was reported in both studies. (17, 18) However, the female subjects who had both pre-conditions were significantly younger than the males. The above finding may be because the female subjects had significantly higher WC values (a risk factor for CVD); as the females increasingly retained abdominal fat from a younger age following early, repeated, poorly spaced pregnancies. Additionally, the females also had significantly lower formal education levels than the males, as low educational attainment may be associated with adverse cardio-metabolic profile. (28, 29)

Subjects with concurrent pre-HTN/DM seemed to have predominantly abnormal 2HPP plasma glucose values, as their FPG values were comparable to values from normal subjects. This buttresses the fact that IGT confers a higher CVD risk similar to T2DM than IFG. (1) The above fact also makes it imperative that an OGTT be done during screening for prediabetes, in addition to FPG so as not to miss out a significant sub-population who might have IGT.

The male subjects had significantly higher DBP values than the females, older age and male gender were significantly associated with prehypertension, while prediabetes had no gender bias but was associated with increasing age. However, increasing age and physical inactivity consistently emerged as a significant predictor of concurrent pre-HTN/DM, in all the logistic regression models.

Dietary practices among the subjects may have contributed to the high prevalence of concurrent pre-HTN/DM evidenced by the daily consumption of raw table salt and sub-par consumption of

fruits/vegetables in majority of the subjects as the above dietary habits are known to be associated with both conditions. (30, 31)

Using the ADA criteria, a very high prevalence of prediabetes (combined IFG and IGT) at 33.5% was found in this Nigerian community as against a prevalence figure of 21.5% in this same community, when the WHO criteria applied. (8)

In addition, IFG became more prevalent than IGT when the ADA criteria applied, a reversal in trend reported for this same community, when the WHO criterion was used. (8) However, no significant gender-based difference in prevalence was found.

Though values were not significant, subjects with prediabetes had higher SBP and DBP values compared to those without prediabetes; increasing age and HBP being established risk factors for prediabetes.

Prehypertension was also highly prevalent in this community as roughly one in every three adults has prehypertension and it was significantly more prevalent in the male subjects than in the females; a consistent finding both locally and elsewhere. (12, 13)

Increasing age was significantly associated with preHTN as BP is known to increase with ageing. In addition, subjects with preHTN had significantly higher plasma glucose values during an OGTT, compared to normal subjects.

The mean BMI of the study population was within normal range. This may be due to the high level of physical activity observed among the subjects. Although the BMI was more significantly associated with prediabetes than prehypertension in the study population, it surprisingly appeared as a predictor of prehypertension in the regression model.

4. CONCLUSION

Findings from this study reveal that one in every ten adults has concurrent pre-DM/HTN, a disturbing revelation in a rural Nigerian community as even higher figures may be recorded in urban cities whose inhabitants embrace a more sedentary and cosmopolitan lifestyle. Public health education is hence critical as well as campaigns for improved dietary practices; improved maternal health and family planning practices for the above trend to be reversed.

The community-based nature of our study and the OGTT performed in the subjects to capture those with IGT were the major strengths of our study. However, the main limitation of our study was its cross-sectional nature, which hindered the establishment of causality unlike longitudinal studies. In addition, glucometers were used to estimate subject's plasma glucose using capillary whole blood, though the reading strips had been pre-set by the manufacturers to report results as the equivalent venous plasma glucose values.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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