The Prevalence of Prediabetes among Hypertensive Patients in Enugu, Southeast Nigeria

I. S. I. Ogbu , C. I. Neboh

SUMMARY

Objective: To determine the prevalence of prediabetes among hypertensive patients under treatment.

***Research Design*:** One hundred hypertensive patients under drug treatment, 40 men and 60 women, aged above 35years and 100 age and sex-matched apparently healthy subjects were used for the study. The patients were on aspirin, nifidepine, frusemide and felodipine as mainline drugs. Venous blood samples were collected after over-night fast and 2 hours after 75g dextrose ingestion.

Main Findings: Twenty-five patients, 10 males 25% and 15 females 25%, had prediabetes giving a prevalence of 25%. Fourteen of them (14%). 4 men and 10 women, had impaired fasting glucose only and 5 (5%) patients; 2 men and 3 women had impaired glucose tolerance only. Six patients (6%) had both IFG and IGT. Unreported diabetes was detected in 14 patients (14%), among whom were 7 men and 7 women. Fifteen patients, (15%), had IFG only, and 5 (5%) patients had IGT only. The mean fasting plasma insulin of the patients was 22.2±19.6μU/ml and the HOMA-IR was 5.1±4.5.

Conclusion: The prevalence of prediabetes among the patients did not exceed reported range but the percentage of unreported diabetes was high. The results highlighted the importance of screening for prediabetes in the hypertensive patient population of the study locality. However, there were no significant differences between the parameters of the patients with IFG and IGT, ($p>0.05$)

Niger Med J. Vol. 50, No. 1, Jan. – March, 2009: 14 – 17.

Key words: Prediabetes, hypetension, impaired glucose tolerance, impaired fasting glucose, insulin resistance, HOMA-IR, unreported diabetes.

INTRODUCTION

Epidemiological studies have provided evidence for the co-existence of hypertension (HBP) and Diabetes Mellitus (DM) and possibly point towards a common predisposing or promotional genetic and environmental factors for both of them[1-3]. Both conditions are often seen together in metabolic syndrome[4-6]. DM has a prolonged imtermediate phase known as prediabetes (PD)[7] characterized by impaired fasting plasma glucose, 5.6-6.9mmol/L and impaired glucose tolerance 2 hours after 75g glucose load, 7.8-11.0mmol/L. 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 cardiovascular complications and DM[8-14]. As the prevalence and incidence of DM increase rapidly worldwide[15] so will the prevalence and incidence of PD increase also since the latter is a phase in the natural history of the former.

Among primary health care patients in Canada, a prevalence of 3.5% was reported[16] and 40% was reported among with polycystic ovarian syndrome[17]. A prevalence of 11.2% was repoted among adults aged 50-59 years[18], 33% for those aged more than 70years[19] in American population.

Since liftestyle changes and drug treatment can slow down or even prevent progression to type 2 DM, screeening for PD in HBP makes sense more so as people with PD are at increased risk for the development of cardiovascular complications independent of progression to type 2 DM[8-12]. Chances of developing DM have been known to decrease by as much as 58% as a result of lifestyle changes[20,21]. Identify HBP patient with PD can have important implications for the intesity of treatment and resultant reduction in cardiovascular morbidity and mortality[14]. This study aims at determining the prevalance of PD as IFG and/or IGT and assessing the insulin resistance status, using the homeostatic assessment model of insulin resistance (HOMA-IR) of hypertensive patients under treatment.

MATERIALS AND METHODS

One hundred registered HBP patients, 40 men and 60 women, aged 35 years and above, of the University of Nigeria Teaching Hospital (UNTH), Ituku-Ozalla, in Enugu State of Southeastern Nigeria, were consecutively recruited for this study. They were all on combined anti-hypertensive therapy with aspirin, nifidepine, frusemide and felodipine as the mainline drugs. Without drug treatment, their diastolic and systolic Blood Pressure (BP) readings were repeatedly above 90mmHg and 140mmHg respectively. BP readings were done using the 1999

From: Department of Medical Laboratory Sciences, Faculty of Health Sciences & Technology, College of Medicine, University of Nigeria, Enugu, Nigeria.

Correspondence: **I. S. I. Ogbu,** Department of Medical Laboratory Sciences, Faculty of Health Sciences & Technology, College of Medicine, University of Nigeria, Enugu, Nigeria. E-mail isiogbu@yahoo.com

WHO/SH guidelines[22]. Known Dm subjects, patients with secondary high BP, pregnant women and patients below the age of 25 years were not included in the study. This is to avoid the influence of these factors on blood glucose.

One hundred age and sex-matched apparently healthy subjects, (40 men) recruited from the immediate community served as control. The Ethics Committee of the Hospital approved the study protocol and informed consent was obtained from all patients. Measurements of their demographic and anthropometric parameters; age (years), weight (kg), height (meters), waist circumference (WC) (cm) and hip circumference (cm) were taken. Their BP readings, as measured on the day of sample collection, were recorded. Body mass index (BM) (kg/m^2) was calculated as weight in kg divided by square of height in meters, HOMA-IR as the product of fasting insulin in µU/ml and fasting plasma glucose in millimole/l divided by 22.5 and waist-hip ratio (WHR) as waist circumference divided by hip circumference.

Five millimeters of fasting blood samples were collected from the ante-cubital vein of the subjects and 2ml was discharged into a fluoride-oxalate bottle for fasting plasma glucose, (FPG) estimation and the rest into a plain bottle for insulin estimation. The subjects were given 75g dextrose in cold water and further 2ml blood sample collected after two hours of administration of sugar for glucose determination. Plasma glucose was assayed by the method of Trinder[23] and insulin by ELISA method using Syntron Bioresearch Microwell Insulin kit. All determinations were done within 24 hours of sample collection.

For statistical analyses, all the hypertensive subjects were grouped into five; patients, control, those with IGT, IFG and unreported DM. Analysis of variance (ANOVA) statistics was used to compare the mean values of the groups and Pearsons correlation statistic was applied to determine the relationship between the parameters. PD was diagnosed as fasting plasma glucose between 5.6 and 6.1mmol/l and/or 2 hour post-prandial glucose between 7.8 and 11.0mmol/l[7].

RESULTS

Twenty-five patients, 10 males (25%) and 15 females (25%), had PD giving a prevalence of 25% among the patients. Fourteen of the patients with PD (14%), (4 men) had IFG only and 5(5) patients (2 men) had IGT only. Six of the patients, (6%), had both IFG and IGT. Unreported DM was detected in 14(14%), of the patients (7 men) with fasting plasma glucose and/or 2 hour post load plasma glucose higher than 6.9 and/or 11.0mmol/l respectively. Out of the 14 patients with unreported DM five had their 2 hour postprandial plasma glucose in the PD range. Among the controls, two persons had IGT while one person had IFG giving a prevalence of 3.0% for PD.

The hypertensive patients had significantly larger WC (96.74±12.84 cm, p<0.0001) higher WHR (0.8942 ± 0.048, p = 0.0003), FPG (5.21 ± 1.99 mmol/l, p = 0.0032) and 2-hour post prandial glucose, (2HPPG) (6.9 ± 3.3mmol/l, p = 0.0003) than the control (86.23 ± 8.24 cm), (0.8587 ± 0.03636), (4.1 ± 0.72mmol/l) respectively (Table 1). There were no significant differences between the parameters of the male and female subjects within the same group. However, male hypertensive subjects had significantly higher WC (95.35 ± 10.4cm, p = 0.0028), larger WHR (0.902 ± .035, p = 0.0003), FPG (5.6 ± 0.027, p = 0.0361) and 2HPPG (7.5 ± 3.8mmol/l, p = 0.0057) than the male control subjects 86.18 ± 9.4 cm, 0.8594 ± 0.026, 4.2 ± 0.61mmol/l, 4.8 ± 0.59mmol/l respectively (Table 1 &2). Similarly, female hypertensive subjects had significantly higher WC (97.67 ± 14.2 cm, p = 0.0067), WHR (0.8892 ± 0.055), FPG (5.0 ± 1.3mmol/l, p = 0.0129), 2HPPG (6.5 ± 2.8 mmol/l, p = 0.0133) than their control counterparts, 86.31 ± 6.8cm, 0.8577 ± 0.026, 4.0 ± 0.70mmol/l and 4.5 ± 0.86mmol/l respectively; (Table 1 &2).

Patients with IFG had significantly higher BMI (30.73kg/m^2, p <0.05) and WC (101.14 ± 13.43cm, p = <0.05) than those with IGT, 27.79 kg/m^2 and 98.86 ± 11.74cm respectively. Anthropometric parameters did not show significant correlation with any of the laboratory parameters. However, BMI correlated with WC (p = 0.0019,) and WHR, (p = 0.0123). The mean fasting plasma insulin of the patients were 21.55 ± 19.43µ/Uml, men 18.08 ± 6.07µ/Uml, and women 21. 12 ± 12.65µ/Uml while those of the control were 21.57 ± 8.54µ/Uml, men 19.92 ± 10.63µ/Uml, and women 19.15 ± 5.51µ/Uml (p > 0.05). The HOMA-IR of the patients were 5.1 ± 4.5, men 4.4 ± 2.5 and women 5.0 ± 3.1 while those of the control were 4.7 ± 2.9, men 4.4 ± 2.3 and women 3.4 ± 1.4, (p> 0.05). The patient with IFG had fasting plasma insulin of 20.2 ± 7.6µ/Uml and HOMA-IR of 5.4 ± 2.0 while the hypertensive patients with IGT had 19.3 ± 4.9µ/Uml and 5.2 ± 1.6 respectively. These values did not differ significantly either between the men and the women or between those with IFG and IGT (p> 0.05).

Table 1: Comparing the anthropometric parameters of the hypertensive patients and controls.

		WC(cm)	WHR	BM(kg/m^2)
ALL	Patients	96.74±12.84	0.894±0.048	27.85±5.39
	Controls	86.23±8.24	0.859±.0364	28.63±87
	p-value	<0.0001	0.0003	0.4469
MEN	Patients	95.35±10.4	0.902±0.035	26.83±4.34
	Controls	86.18±9.38	0.859±0.043	28.29±2.66
	p-value	0.0028	0.0003	0.2020
WOMEN	Patients	97.67±14.25	0.889±0.55	28.53±5.92
	Controls	86.31±6.84	0.858±.027	29.08±3.17
	p-value	0.0067	0.0503	0.7499

Table 2: Comparing the laboratory parameters of the hypertensive patients and controls.

		FPG (mmol/l)	2HPPG (mmol/l)	FPI (µU/ml)	HOMA-IR
ALL	Patients	5.21±2.0	6.9±3.3	21.55±19.43	5.1±4.5
	Controls	4.1±0.64	4.7±0.72	21.57±8.54	4.7±2.9
	p-value	0.0032	0.0003	1.994	0.1946
MEN	Patients	5.6±2.7	7.1±3.8	18.08±6.07	4.4±2.5
	Controls	4.2±0.61	4.8±0.60	19.92±10.63	4.4±2.3
	p-value	0.0361	0.0057	0.0173	0.5661
WOMEN	Patients	5.0±1.3	6.5±2.8	21.12±12.65	5.0±3.1
	Controls	4.0±0.70	4.5±0.86	19.15±5.51	3.4±1.4
	p-value	0.0129	0.0133	0.5860	0.0845

Table 3: Clinical Characteristics of the different groups of hypertensive patients and control.

	All Patient (N=100)	IFG (N=14)	IGT (N=5)	Prediabetes (N=25)	Unreported diabetes (N=14)	control (N=100)
Age (years)	56.8±11.1 (35–75)	56.1±10.95 (37–70)	61±9.7 (52–65)	57.5±9.9 (37–75)	54.9±10.8 (36–70)	51±10.9 (35–70)
BMI (kg./m^2)	27.85±5.39 (16–42)	30.7±5.3 (21–40)	27.79±5.7 (21–34)	29.4±5.3 (21–40)	26.8±5.3 (19–37)	28.7±3.2 (23–35)
WC (cm)	96.74±12.84 (74–130)	101.14±13.4 (76–116)	98.86±11.7 (89–114)	98.7±12.6 (76–116)	96.4±10.7 (76–111)	86.23±8.24 (72–109)
WHR	0.894±0.048 (.76–0.97)	0.9±0.6 (.81–.96)	0.91±.04 (.88–.97)	0.91±0.04 (.79–.97)	0.91±.03 (.85–.94)	0.859±0.0364 (.78–.91)
FPG (mmol/l)	5.21±2.0 (2.2–19.4)	6.02±0.45 (5.6–6.3)	5.7±1.85 (3.5–4.8)	5.96±0.9 (3.5–6.9)	8.5±3.3 (5.6–19.4)	4.1±0.64 (3.1–5.6)
2HPPG (mmol/l)	6.9±3.3 (3.2–24.6)	7.24±1.63 (4.8–7.7)	8.8±0.82 (7.9–10.4)	7.7±1.68 (4.8–10.4)	13.1±4.4 (8.3–24.6)	4.7±0.72 (3.1–6.1)
FPI (μU/ml)	21.55±19.43 (8.6–104)	20.2±17.6 (11.8–48.2)	19.21±5.26 (10.6–0.4)	19.45±7.1 (10.7–48.2)	21.1±6.4 (9.6–32.1)	21.57±8.54 (13.9–53.6)
HOMA-IR	5.1±4.54 (1.2–18.5)	5.41±2.02 (2.7–11.2)	5.2±1.69 (2.1–4.7)	5.1±2.0 (2.1–11.2)	7.1±2.4 (3.7–11.6)	4.7±2.9 (2.0–11.1)

±SD; (Range)

DISCUSION

The prevalence of PD among the HBP patients of the UNTH was 25%. This is within the range of 25 - 47% reported by Giovindarajan *et al* [24]. Shrestha et al reported a prevalence of 43% among hypertensive patients in urban Nepal[25]. Mills and Grant stated that 25% of the population was in state of relative insulin resistance which preceded type 2 DM[26]. A prevalence of 3.5% was reported among primary health care patients with illness in Canada[19], and 40% of women with polycystic ovarian syndrome [20]. Although 25% of US adults were known to have PD, only an estimated 4% were aware of this[27,28]. Awareness was not assessed in this study. However, lack of the knowledge of the existence of PD in an individual makes screening for the condition in the general population necessary.

Impaired fasting glucose was more prevalent among the patients 15%, than IGT (5%). This is contrary to the report of Shobha et al who recorded a prevalence of 9.7% for IFG and 15.6% for IGT in US adult aged 40 -74 years. Among overweight subjects aged 45 - 74 years, the prevalence of combined IFG and IGT in Penghu Islets of Taiwan was found to be 14.7% and 30.7% among the women and men within the age ranges of 40 - 49 years and 50 - 59 years respectively [29].

IGT was said to be more sensitive in detecting early dysregulation than IFG. It reflects hepatic gluconeogenesis and slower uptake to glucose from blood into skeletal muscles and adipose tissue following a meal [30]. It is also independently associated with traditional microvascular complications of diabetes. IGT patients, however, will not always progress to diabetes since it is a dynamic and reversible state. Some will revert to normoglycaemia while a greater percentage may continue as such [30]. Six patients (6%) had both IFG and IGT. Eleven patients, therefore, had IGT in this study (5 IGT alone and 6 IGT plus IFG), and are at increased risk of progressing to type 2 DM and developing cardiovascular disorders.

A large number of the patients (14%) had unreported DM. This underscores the necessity for regular screening of HBP patients for DM. The mean HOMA-IR of the patients, (5.1 ± 4.5) is in the upper range of values reported for PD (4.3 - 5.2) with some definitely in the DM range, 8.3 - 9.5, due to the presence of the unreported DM subjects. The HOMA-IR of the control subjects was ouside the range of values reported for White Americans, 2.1 - 2.7 (31). The prevalence of PD among the patients did not exceed reported value range but the percentage of unreported DM was high. The reasons may include ignorance and lack of affordable health services. The lack of correlation between the anthropometric parameters and the laboratory parameters indicates that it may not be possible to predict PD from knowledge of the former parameters. The patients did not differ significantly from the control in their BMI but not in elevated WC and WHR. The differences in the later parameters reflect in significantly elevated fasting and 2-hour post prandial plasma glucose of the patients. This shows that BMI is not a good index of obesity in this group of patients. Normal fasting insulin levels in the hypertensive patients reflect the fact that most of the patients could secret enough insulin to keep them in normogycaemic state in the absence of insulin resistance as shown by normal index of insulin resistance.

The study has highlighted the importance of screening

for PD especially among HBP patients of the study locality.

REFERENCES

1. El-Atat F., McFarlane S. I., Sowers J.R. Diabetes, hypertension, and cardiovascular derangements: pathophysiology and management. *Curr Hypertens Rv* 2004; **6(3):** 215 – 221.
2. Sowers J. R., Epstein M., Frohlich E. D. Diabetes, hypertension, and cardiovascular diseases: an update. *Hypertension* 2001; **37(4):** 1053 – 1059.
3. Sowers J. R., Epstein M. Diabetes mellitus and associated hypertension, vacular diseas and nephropathy. An update. *Hypertension* 1995; **26 (6 pt 1):** 869 – 879.
4. National High Blood Pressure Education Programme Working Group report on hypertension in diabetes. *Hypertension* 1994; **23(2):** 145–158.
5. Shobha S. R. Philip S., Tamara M., Impaired glucose tolerance and impaired fasting glucose. *Am Fam Physician* 2004; **69(8):** 1961–1968, 1971 – 1972.
6. Executive Summary of the third report of the National Cholesterol ducation Programme, (NCEP), Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults, (Adult Treatment Panel 111). *JAMA* 2001; **285(23):** 2486 – 2497.
7. Ramlo-Halsted B. A., Edelman S. V. The natural history of type 2 diabetes: implications for clinical pratice. *Prim Care* 1999; **26(4):** 771–789.
8. Edelstein S. L., Knowler W. C. Bain R. P. et al. Predictors of progression from impaired glucose tolerance to NIDDM: an analysis of six perspective studies. *Diabetes* 1997; **46(3):** 701–710.
9. Robinson S. J., Gordon S. A., Russell J. W., Feldman E. L. Microvascular complications of impaired glucose tolerance. *Diabetes* 2003; **52(15):** 2867– 2873.
10. Tominage M., Eguchi H., Igarashi K., Kato T., Sekikawa A. Impaired glucose tolerance is a risk factor for cardiovascular disease, but not impaired fasting glucose: the Funagata Diabetes Study. *Diabetes Care* 1999; **222(6):** 920 – 924.
11. Kuller L. H., Veletgas P., Barzilay J., Beauchanp N. J. O'Leary D. H., Savage P. J. Diabetes mellitus: subclinical cardiovascular disease and risk of incident mortality. *Arterioscer Thromb Vasc Biol* 2000; **20(5):** 823 –829.
12. The DECODE Study: Group for the European Diabetes Epidemiology Group Glucose tolerance and cardiovascular mortality: comparison of fasting and two hour diagnostic criteria. *Arch Intern Med* 2001; **161(3):** 397 – 405.
13. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Clinical Practice Guideliness for the Prevention and Management of Diabetes in Canada. Screening and Prevention. *Can J Diabetes* 2003; **27(Suppl 12):** S10–S13.
14. Harris R., Donahue K., Rathore S. S., Frame P., Woolf S. H., Lohr K. N. Screening adults for type 2 diabetes: a review of the evidence for the US Preventive Services Task Force. *Ann Intern Med* 2003; **138(3):** 215 – 229.
15. Borch-Johnsen K., Lauritzen T., Glumer C., Sandback A. Screening for type 2 diabetes-should it be now? *Diabetes Med* 2003; **20(3):** 175–181.
16. Leiter L. A., Barr A., Belanger A., Lubin S., Ross S. A. Tildesley H. D. *et al*, Diabetes screening in Canada, (DIASCAN), Study: prevalence of undiagnosed diabetes and glucose intolerance in family physician offices. *Diabetes Care* 2001; **24(6):** 1038 – 1043.
17. Lord J. M., Flight I. H., Norman R. J. Metformn in polycystic ovarian syndrome; systematic review and metanalysis. *BMJ* 2003; **327(7421):** 951 – 953.
18. Harris M. I., Flegal K. M., Cowie C. C., Eberhardt M. S. Goldstein D. E., Little R. R., Weidmeyer H. M., Byrd-Holt D. D. Prevalence of diabetes, impaired fasting glucose and impaired glucose tolerance in US adults. *Diabetes Care* 1999; **21(4):** 518 – 524.
19. Hiltunen L., Laara E., Keinane-Kuikaaniemi S. Changes in glucose tolerance during a three year's follow-up in an elderly population. *Public Health* 1999; **13(2):** 181 – 184.
20. Pan X. R., Li G. N., Hu Y. H., Wang J. X., Yang W. Y., A Z. X., *et al.* Effect of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Quig IGT and Diabetes Study. *Diabetes Care* 1997; **29(4):** 537 – 544.
21. Tuomilehto J., Lindstrom J., Eriksson J. G., Valle T. T., Hamalainen H., Illanne-Parikka P., *et al.* Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001; **344(18):** 1343 – 1350.
22. WHO/ISH Guidelines for the Management of Hypertension. *J Hypertens* 1999; **17:** 151 – 183.
23. Trinder P. Determination blood glucose using an oxidase-peroxidase system with a non-carcinogenic chromogen. *J. Clin. Pathol.* 1969; **22:** 158 – 161.
24. Diabetes Prevention Programme Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J. Med.* 2000; **346(6):** 393 – 463.
25. Chiasson J. L., Gomis R., Hanefeld M., Josse R. G. Karasik A., Laakso M. The STOP NIDDM Trail: an international study on the efficacy of alpha-glucosidase inhibitor to prevent type 2 diabetes in a population with impaired glucose tolerance: rationale, design and preliminary screening data. Study to Prevent Non-Insulin Dependent Diabetes Mellitus. *Diabetes Care* 1998; **21(10):** 1720 – 1725.
26. Govindarajan G., Sowers J. R., Stump C. hypertension and diabeted mellitus, 2006. Available at: http://www.touchcardiology.com/articles/hypertension-and-diabetes-mellitus.
27. Shrestha U. K., Singh D. L., Bhattarai M. D. The prevalence of hypertension and diabetes defined buy fasting and 2 hour plasma glucose criteria in urban Nepal. *Diabetes Medicine* 2006; **23(10):** 1130 – 1135.
28. Chen K., High L. Prevalence f impaired fasting glucose and type 2 diabetes mellitus in Benghu Islets, Taiwan: evidence of a rapidly emerging epidemic. *Diab Res Clin Pract* 2009; **44(1):** 59 – 69.
29. Mills J. D., Grant P. J. Insulin resistance homeostasis factors and cardiovascular risk. *Br J Diabetes Vasc Dis* 2000; **2(1):** 19 – 26.
30. American Diabetes Association. Standards of medical care in diabetes - 2008. *Diabetes Care* 2008; **31(Suppl 1):** S12 –S54.
31. Rolka D. R., Burrows N. R. Li Y., Geiss L. S. Self-reported prediabetes and risk-reduction activities-US-2006. *JAMA* 2009; **301(6):** 591 – 593.
32. Singleton J. R., Smith A. G., Russel J. W., Feldman E. L. Microvascular complications of impaired glucose tolerance. *Dabetes* 2003; **52(14):** 2867 – 2873.
33. Adediran O. S., Jimoh A. K., Ogbera A. O. Metabolic syndrome: the pathogenesis of its predictors. *Postgraduate Doctor* **22(2):** 35 – 45.