Undiagnosed diabetes mellitus and impaired glucose tolerance among hypertensive patients in Mulago Hospital, Kampala, Uganda

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Abstract

Both diabetes and impaired glucose tolerance (IGT) are rising globally, and are known to be associated with hypertension. We have assessed the prevalence of, and risk factors for, abnormal glucose tolerance (AGT) among hypertensive patients in Kampala, Uganda. A total of 320 randomly chosen hypertensive patients were studied, demographic and other data collected, and an oral glucose tolerance test (OGTT) carried out. AGT was found in 237 (74%) patents – 50% had IGT and 24% type 2 diabetes. The following factors were significantly associated with AGT: body mass index (BMI) over 28.0 kg/m^2 (p=0.003), family history of diabetes (p=0.002), physical inactivity (p=0.001), alcohol consumption (p=0.01), and a systolic blood pressure (BP) over 140 mmHg. We conclude that diabetes and IGT are highly prevalent in hypertensive patients and screening for these conditions in such patients should be considered.

Introduction

Diabetes mellitus is a growing problem worldwide with rising prevalence rates,[1] including in sub-Saharan Africa.[2,3] The global rise in type 2 diabetes is occurring fastest in developing countries.[4,5] This is all compounded by the fact that as many as 50% of people with diabetes are yet to be diagnosed. The World Health Organization (WHO) estimated that there were 314 million people worldwide with the intermediate state of impaired glucose tolerance (IGT), and this is expected to rise to 500 million by 2015.[6,7]

Patients with pre-diabetes states have a higher risk for development of overt diabetes since they form an intermediate stage in its natural history.[8] In an analysis of six prospective studies, Edelstein et al, found a risk of 3.6 to 8.7% per year for type 2 diabetes development in patients with IGT. Elevated fasting glucose levels, elevated 2-hour challenge glucose values and a body mass index (BMI) greater than 27 kg/m^2 were associated with the development of diabetes in these patients.[9] They therefore form a very important target group for primary prevention as well as identification of diabetic complications that usually precede its diagnosis by 4–7 years.

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Risk factors for development of IGT have been described, and include:

- the metabolic syndrome (or insulin resistance syndrome in which hypertension is a key factor);
- lack of exercise;
- age over 45 years;
- family history of diabetes;
- history of gestational diabetes or delivery of a baby weighing over 4.1 kg;
- smoking.[9,10]

It is well known that hypertension frequently occurs with diabetes. Possible explanations include higher homocysteine levels and greater insulin resistance in hypertension.[10] Korhonen et al in a study of 1066 hypertensives found diabetes in 66 (6%), IGT in 220 (20%), and impaired fasting glucose (IFG) in 167 (15%).[11] We have therefore carried out the present study in Uganda, to examine the rates of diabetes and IGT in a hypertensive population.

Patients and methods

A cross-sectional descriptive study design was used to estimate the glucose tolerance and factors associated with it among hypertensive patients attending the Mulago Hospital outpatient Hypertension Clinic. Mulago Hospital is Uganda's national referral and university teaching hospital, and is located in the capital city Kampala. The hospital also serves as a primary health unit for patients in nearby districts of Kampala.

Sample size estimation was based on a prevalence of IGT among ischaemic heart disease patients and hypertensive patients of 21% as reported by Savage et al.[12] Patients meeting inclusion criteria were selected by systematic random sampling using the outpatient registry in the Hypertension Clinic. Informed consent was obtained using a written informed consent process. Febrile patients, those allergic to commercially prepared glucose, those previously diagnosed with diabetes, and

pregnant women were excluded. Consenting subjects were then booked for an oral glucose tolerance test (OGTT) in a week's time. They were advised to take an unrestricted diet and to fast for 8 hours on the evening of the test. Using these procedures, 320 consenting adult hypertensives were recruited.

A standardised questionnaire was used to collect measurements on the history, clinical examination and laboratory investigations. Blood was collected for fasting blood glucose and during the OGTT. All blood glucose levels were determined using glucometers and finger prick capillary blood specimens (Medisense-Precision manufactured by Abbott Laboratories). After the OGTT, patients were categorised as normal, IGT, and diabetes using the American Diabetes Association and WHO criteria.[1,6] All clinically significant abnormalities were communicated to the attending physicians for further treatment and follow-up.

Data were entered into EPI-INFO Version 6 and analysed using SPSS 13. Proportions for the different factors were obtained. Their odds ratios (95% confidence interval (CI), p value) were also determined using the Chi-square test. Those with a p value less than 0.05 were subsequently used in multivariate analysis. Positive associations were considered if the odds ratio was greater than 1.0 and p< 0.05.

Approval was acquired from the Department of Internal Medicine, Makerere University and ethics approval was obtained from the Faculty of Medicine Research and Ethics Committee.

Results

From November 2005 to February 2006, 393 patients were approached for consent to participate in the study and 320 were recruited. Of the 73 excluded, 61 already had diabetes, 4 did not consent, while 8 withdrew from further evaluation after consenting.

Demographic characteristics. These are shown in Table 1. The main finding of interst was that 226 (73%) of the patients were female.

Clinical and lifestyle characteristics. These are shown in Table 2. Some 58% of subjects had a BMI >28.0. A significant number of patients (49%) had been dignosed with hypertension below the age of 45 years.

Prevalence of glucose intolerance. The prevalences of normal glucose tolerance, impaired glucose tolerance, and diabetes were 26% (n=83), 50% (n=160), and 24% (n=77), respectively as shown in Figure 1. Only 50% of subjects had normal glucose tolerance.

Risk factors and associations with abnormal glucose tolerance (AGT) at bivariate analysis. These are shown in Table 3. Patients over 45 years of age were more likely to have AGT at the time of diagnosis of hypertension than those less than 45 years (80% vs. 68%, p=0.005). Those who had used bendrofluazide or atenolol were more likely to have AGT than those who had not (85% vs. 66%, p=0.001 and 94% vs. 67%, p<0.001), respectively.

Other positive associations with AGT included a BMI >28.0 (p=0.03), females who had delivered a baby >4.1 kg (p<0.001), family history of diabetes (p=0.008), family history of obesity (p=0.001), living with a smoker (p<0.001), lack of exercise (p<0.001), and a systolic BP >140 mmHg (p=0.021). Factors not associated with AGT included age, gender, cigarette smoking, and frequency of exercise.

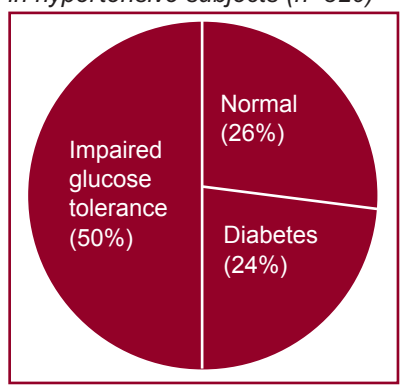
Factors associated with AGT on multivariate analysis

Factors that were found significant on bivariate analysis were further tested in binary logistic regression. The results are shown in Table 4. Significant associations were found with a BMI>28.0, a family history of diabetes, alcohol use, physical inactivity, and systolic BP level.

Table 1 Demographic characteristics of the study population (n=320)

Parameter	Frequency (%)
Tribe	
Baganda	83%
Others	17%
Age (years)	
<45	20%
>45	80%
Religion	
Christian	74%
Muslim	22%
Other.	4%
Sex	
Female	73%
Male	27%
Education	
None/primary	66%
Secondary/tertiary	34%
Employment	
None	54%
Present	46%
Marital status	
Married/cohabiting	49%
Widowed	23%
Divorced/separated	22%
Never married	6%

Figure 1 Glucose intolerant states in hypertensive subjects (n=320)



Discussion

Our study found very high rates of undiagnosed diabetes and IGT (50%) among our hypertensive cohort. Only 26% had entirely normal glucose tolerance.

This is the first study in Uganda to establish the magnitude of this problem. Omar et al found that only 23% of their 1064 hypertensive patients had normal glucose tolerance in Durban, South Africa.[14] Other studies in Europe have showed lower rates. Savage et al in Britain screened for glucose tolerance among 327 hypertensive and ischaemic heart disease patients and found 3% had diabetes while 18% had IGT.[12] Similarly Luders et al in Germany found the prevalence of diabetes and IGT to be 12% and 39% respectively.[14] Lower rates of undiagnosed

Table 2 Clinical and lifestyle characteristics of the study population (n=320)

Parameter	Frequency
Duration of hypertension (years)	
<10	62%
>10	38%
Age at diagnosis of hypertension (years)	
<45	49%
>45	51%
Body mass index	
<28	42%
>28	58%
Female delivering baby of (kg)*	
<4.1	63%
>4.1	37%
Family history of diabetes	
Yes	33%
No	77%
Family history of obesity	
Yes	45%
No	55%
Alcohol use duration (years)**	
<4	79%
>4	21%
Cigarette smoking	
Yes	5%
No	95%
Living with smoker	
Yes	16%
No	84%
Exercise	
Yes	12%
No	88%
Systolic BP (mmHg)	
>140	71%
<140	29%
Atenolol use	
Yes	27%
No	73%
Bendrofluazide use	
Yes	45%
No	55%

Note * For females delivering baby/babies < or >4.1 kg, n was 234.
** For alcohol duration, n was 98.

glucose intolerance and diabetes are expected in the developed nations because of their better glucose testing programmes. The higher rates in developing nations, as in our study, are largely due to the absence of rigorous screening, leaving many patients undiagnosed.

The factors statistically associated with AGT after both secondary and binary logistic regression in our study were a BMI over 28 kg/m^2, family history of diabetes, alcohol consumption, physical inactivity, and systolic BP over 140 mmHg. The risk factors earlier described by the ADA include the above, except that our study did not find age over 45 years, delivery of a baby over 4.1 kg and diastolic BP over 90 mmHg to be significant risk factors.[5] Similar findings to ours were demonstrated by Wang et al[15] who investigated risk factors for glucose intolerance in the Hubei province of China. In this study, abnormal glucose tolerance was significantly related to a family history of type 2 diabetes, hypertension, high BMI, and age. This concordance of results emphasises the association between obesity, hypertension, and AGT

We demonstrated a significant association between alcohol consumption and AGT. The relationship between alcohol consumption and AGT is multi-factorial and may involve genetic and environmental factors and pancreatitis. We found physical inactivity to be a significant risk factor for AGT in our study. Exercise increases insulin sensitivity.[16] Levitt et al also demonstrated that low total energy expenditure was a significant risk factor for diabetes and glucose intolerance among 974 patients in South Africa.[17] Our study showed that a family history of diabetes was a strong risk factor for glucose intolerance among hypertensives. Elbagir and colleagues, in their study of 724 subjects from a community of high diabetes prevalence in Sudan, also showed strong association between family history of diabetes and AGT.[18] We established that a raised systolic BP was a risk factor for AGT. Similar findings were found by Omar et al who showed a trend of increasing glucose intolerance as BP rose.[13] Our study did not establish increasing age and sex as significant risk factors, unlike Omar et al[13] and Richard et al.[19] This could have been due to fact that our study subjects were skewed towards a predominantly female population. Other factors noted previously by other authors, but which were not significant risk factors in our study included smoking and large babies.[20]

In conclusion, our study found very high rates of undiagnosed diabetes and IGT among hypertensive subjects in Kampala, Uganda. It also established that raised BMI, a family history of diabetes, alcohol consumption, physical inactivity, and raised BP were significantly associated with AGT. There is a strong case for diabetes screening amongst hypertensive patients.

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Table 3 Risk factors and their associations with abnormal glucose tolerance (AGT) by bivariate analysis

Character	AGT (n=237)	Normal (n=83)	p value	Odds ratio (95% CI)
Age (years)				
>45	49	15	0.203	1.600
<45	188	68		(0.774–3.295)
Sex				
Female	179	55	0.239	1.500
Male	58	28		(0.757–3.029)
Age at diagnosis of HT (years)				
>45	130	33	0.050	1.100
<45	107	50		(1.100–3.656)
Bendrofluazide use				
Yes	124	21	0.001	3.220
No	113	62		(1.584–6.543)
Atenolol use				
Yes	81	5	<0.001	1.420
No	156	78		(1.242–1.622)
BMI				
>28	150	37	0.030	2.252
<28	87	46		(1.638–3.458)
Delivered baby >4.1 kg				
Yes	79	8	<0.001	1.405
No	100	47		(1.189–1.660)
Family history of diabetes				
Yes	90	15	0.008	2.852
No	147	68		(1.289–6.310)
Family history of obesity				
Yes	123	21	0.001	3.132
No	114	62		(1.541–6.364)
Alcohol use				
Yes	93	5	<0.001	1.468
No	144	78		(1.280–1.684)
Alcohol use duration (years)				
>4	75	2	0.050	1.157
<4	18	3		(1,1–1.464)
Cigarette smoking				
Yes	13	3	0.656	1.431
No	224	80		(0.294–6.970)
Living with a smoker				
Yes	50	2	0.001	1.394
No	187	81		(1.237–1.570)
Exercise				
Yes	7	30	<0.001	3.723
No	230	53		(1.709–8.111)
Exercise				
>3 x weekly	5	26	0.132	0.188
<3 x weekly	2	4		(0.019–1.900)
Systolic BP (mmHg)				
>140	179	49	0.021	2.200
<140	58	34		(1.120–4.321)

Table 4 Risk factors significantly associated with abnormal glucose tolerance (AGT) on binary logistic regression analysis

Variables	Significance	Odds ratio	95% CI
BMI ≥ 28.0	0.003	1.5	1.31–1.92
Family history of diabetes	0.002	2.2	1.91–2.52
Alcohol use	0.01	1.2	1.12–1.45
Physical inactivity	0.001	2.9	1.80–4.25
Systolic BP	0.042	1.3	1.02–1.62

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