



## RELATIONSHIPS BETWEEN DEMOGRAPHIC VARIABLES AND DISORDERS OF GLUCOSE METABOLISM IN APPARENTLY HEALTHY NIGERIANS

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### ABSTRACT

**Background:** A latent period of abnormal glucose metabolism precedes type 2 diabetes and it is associated with cardiovascular complications. Factors that facilitate progression into diabetes may include older age, over-weight and existence of other diabetes risk factors. This study determined the effects of advancing age, sex and weight on the development of glucose metabolism disorders in apparently healthy Nigerian. **Methodology:** 1,012 apparently healthy subjects aged 45 years and above were recruited for the study. Their anthropometric parameters were measured using standard methods and plasma glucose was measured using glucose oxidase method. Diagnosis of diabetes and pre-diabetes was made according to WHO criteria. **Results:** A total of 173 subjects had pre-diabetes, (PD), giving a prevalence of 17.0%. its prevalence declined from 18.4% in the 4<sup>th</sup> decade to 15.6% in the 5<sup>th</sup>, 9.6% in the 6<sup>th</sup> and then increased to 41.9% in the 7<sup>th</sup> decade and beyond, of life. The highest prevalence of impaired fasting glycaemia, (IFG), was recorded in the 4<sup>th</sup> decade of life while that of impaired glucose tolerance, (IGT), occurred in the 5<sup>th</sup>. A slightly greater percentage of males, 17.9%, than females, 16.7%, had pre-diabetes. In the male group, pre-diabetes was common in the 4<sup>th</sup> and 7<sup>th</sup> decade while in the female group prevalence was more evenly distributed through the years. Unreported diabetes was detected in 87 subjects, giving a prevalence of 8.6% of the study population, most of them in the 50 – 69 years age bracket. It was more prevalent in the female subjects, 11.1% than in the male subjects 4.4%. among the male pre-diabetes subjects, peak values for these parameters occurred much earlier, 40 – 59 years range. **Conclusion:** The report showed high prevalence of abnormal glucose metabolism and un-reported diabetes mellitus (URDM), in the apparently healthy population. Age, sex and weight affect glucose metabolism adversely. IGT is a better predictor of future diabetes than IFG and the 5<sup>th</sup> decade of life is most crucial in the progression of PD to diabetes. Screening for glucose metabolic disorders is better done using OGTT/2hppG than FPG. The need for regular screening of the population for glucose intolerance was highlighted in order to reduce the incidence of diabetes and its complications.

**KEYWORDS:** Pre-diabetes, un-reported diabetes mellitus, impaired fasting glycaemia, impaired glucose tolerance, age, sex, weight.

### INTRODUCTION

A latent period of abnormal glucose metabolism; impaired glucose tolerance (IGT) and impaired fasting glycaemia (IFG), often precede type 2 diabetes.<sup>[1]</sup> These are metabolic states between normal glucose homeostasis and diabetes and are termed pre-diabetes, (PD). The gap between PD and development of clinical diabetes vary between individuals and could be as long as  $\geq 10$  years. Because pre-diabetes is not a clinical entity, it may progress to diabetes without the sufferer being aware of it-unreported diabetes mellitus, (URDM).

URDM and PD are considered to have substantial clinical importance.<sup>[2,3]</sup> Subjects with pre-diabetes, though apparently healthy, have increased risk of macro-vascular complications.<sup>[4,5]</sup> They have normal or near-normal glycated haemoglobin.<sup>[6]</sup> IGT manifests hyperglycaemia only when standard oral glucose tolerance test (OGTT) is performed. It may be directly involved in the pathogenesis of cardiovascular disease (CVD) and has a higher risk for CVD than IFG.<sup>[7]</sup> IFG and IGT are associate with insulin resistance and impaired insulin secretion,<sup>[8,9]</sup> However, there are differences in the nature of these defects between the two conditions.<sup>[8]</sup>

Not all individuals with pre-diabetes progress to diabetes. 50% remain in their abnormal glycaemic state, 25% revert to normal glucose tolerance leaving 25% to progress to diabetes over an observational period of 3-5 years,<sup>[4,10,11]</sup> IGT and IFG have heterogeneous pathogenesis and different rates of progression to diabetes.<sup>[12,13]</sup> Factors that facilitate progression into diabetes include older age, over-weight and existence of other diabetes risk factors.<sup>[14]</sup> There are yet no reports of the effect of advancing age, gender and weight on the development of both PD and URDM among Nigerian.

## MATERIALS AND METHODS

The study was carried out in Owerri Municipality of Imo State of Nigeria. The inhabitants are mainly Igbos and it has a population of 125,337 (2006 Census in Nigeria). The study was approved by the Ethic Committee of The Federal Medical Centre, Owerri and involved a total of 1,012 apparently healthy adults (males 273, females 739) aged > 45 years. Informed consent was obtained from all subjects before sample collection. Pregnant women were excluded. Fasting and 2 – hour post-prandial blood samples were obtained using standard methods,<sup>[15]</sup> and put into fluoride-oxalate bottle for glucose estimation which was done within 2 hours blood sample, subjects received 75g of glucose-D dissolved in 250 – 200ml water over a period of 5 minutes.

Anthropometric measurements of height, weight, waist and hip circumference (WC, HC) were taken using standard methods,<sup>[16]</sup> Body weight in light clothing was measured to the nearest 0.1kg using electronic scale. An average of two readings was taken. Height was measured to the nearest 0.5cm using vertically mounted measuring device. Body mass index (BMI), was calculated as weight in kilograms divided by square of height in meters, (kg/m<sup>2</sup>). Waist circumference was measured to the nearest 0.5cm at a level midway between the lowest rib and the iliac crest using measuring tape. Waist to hip ratio (WHR) was also calculated.

Data were grouped in decades of life starting from 40 – 50 to ≥ 70 years and analyses were done using GraphPad software. Continuous variables were compared using Student's "t" test and ANOVA statistics and results were presented as mean ± standard deviation or as count and percentage of status or category. Pre-diabetes was diagnosed as impaired fasting glycaemia (IFG), FPG 5.6 – 6.9mmol/l, 2hpp glucose < 11.0mmol/l, as IGT, FPG < 6.9mmol/l, 2-hpp glucose 7.7 – 10.9mmol/l. Diabetes as

FPG >7.0mmol/l and /or 2-hpp glucose > 11.0mmol/l; normal glucose tolerance (NGT) as, FPG <5.6mmol/l, 2-hpp glucose < 7.7mmol/l; IFG alone as, FPG 5 – 6.9, 2-hppG < 7.7mmol/l; IGT alone as, FPG <5.6mmol/l, 2-hppG 7.7 – 10.9mmol/l.<sup>[20]</sup>

## RESULTS

A total of 173 subjects had pre-diabetes giving a prevalence of 17.0%. Prevalence declined from 18.4% in the 4<sup>th</sup> decade to 15.6% in the 5<sup>th</sup>, 9.6% in the 6<sup>th</sup> and then increased to 41.9% in the 7<sup>th</sup> decade and beyond, of life (Table 2). Similar pattern was observed in the male group but the rate in the 4<sup>th</sup> and 7<sup>th</sup> decades were same – 27%, (Table 3) while in the female group prevalence rate was rather sustained in the 4<sup>th</sup> and 5<sup>th</sup> decades, decreased in the 6<sup>th</sup> and rose to near 100% in the 7<sup>th</sup> decade of life, (Table 4). Generally, lowest prevalence rates were recorded in the 60 – 69 years of life and highest thereafter. A slightly greater percentage of males, 17.9%, than females, 16.7%, had pre-diabetes. In the male group, pre-diabetes was common in the 4<sup>th</sup> and 7<sup>th</sup> decade while in the female group prevalence was more evenly distributed though the years, (Table 3 & 4).

87 (8.6%) subjects had unreported diabetes mellitus (URDM) with FBG > 7.0mmol/l and /or 2 hour postprandial glucose >11.1mmol/l. Most of them, (58; 66.7%) were in the 5<sup>th</sup> decade of life, (Table 2). More women (75, 86.2%), than men, (12, 13.8%), had URDM, (Table 3 & 4). In the male group, URDM occurred only in the 50 – 69 years age bracket while the condition was detected from 40 to 69 years of age in the female subjects (Table 3 & 4).

The highest prevalence of IFG was recorded in the 7<sup>th</sup> decade and beyond while that of IGT occurred in the 5<sup>th</sup>. (Table 2) A Combination of IFG and IGT occurred rarely in the study population, (11; 10%) and none was detected after the 5<sup>th</sup> decade of life (Table 2).

Mean values of BMI and WHR were highest in the 5<sup>th</sup> decade of life, 29.0 ± 4.2 kg/m<sup>2</sup> and 1.02 ± 0.1 respectively. Generally, the women were heavier and had higher blood glucose values than the men, (Table 1).

**Table 1: Clinical characteristics of the study population; number in bracket.**

| Parameter                | Whole population (1,012) | Males (273) | Females (739) | P-value (M vs F) |
|--------------------------|--------------------------|-------------|---------------|------------------|
| Age (years)              | 56 ± 8.5                 | 59.9 ± 10.7 | 54.5 ± 7.0    | > 0.05           |
| BMI (Kg/m <sup>2</sup> ) | 28 ± 4.4                 | 26.3 ± 2.7  | 28.6 ± 4.4    | < 0.05           |
| WHR                      | 0.97 ± 0.1               | 0.97 ± 0.1  | 0.97 ± 0.1    | > 0.05           |
| FGT (mMol/l)             | 4.76 ± 1.9               | 4.6 ± 1.9   | 4.8 ± 1.9     | < 0.05           |
| 2HPPG (mMol/l)           | 6.93 ± 3.7               | 5.96 ± 2.8  | 7.29 ± 3.9    | < 0.05           |

**Table 2: Prevalence (%) of IFG, IGT, IFG + IGT, URDM in the whole study population and variation with age; number in bracket.**

| Condition    | 40 – 49 Year (300) | 50 – 59 years (371) | 60 – 69 years (260) | ≥ 70 years (81) | Total (1,012) |
|--------------|--------------------|---------------------|---------------------|-----------------|---------------|
| IFG alone    | (27) 9.0           | (2.0) 0.5           | (2.0) 0.8           | (32) 39.5       | (63) 6.2      |
| IGT alone    | (23) 7.7           | (51) 13.7           | (23) 8.8            | (2) 2.4         | (99) 9.8      |
| IFG + IGT    | (5) 1.7            | (6) 1.6             | (0) 0               | (0) 0           | (11) 1.0      |
| Pre-diabetes | 550) 18.4          | (59) 15.8           | (25) 9.6            | (34) 41.9       | (173) 17.0    |
| URDM         | (7) 2.3            | (58) 15.6           | (22) 8.4            | (0) 0           | (87) 8.6      |
| NGT          | (238) 79.3         | (254) 68.4          | (213) 81.9          | (47) 58         | (752) 74.3    |

**Table 3: Prevalence (%) of IFG, IGT, IFG + IGT, URDM and NGT in the male population and variation with age; number in bracket.**

| Condition    | 40 – 49 Year (74) | 50 – 59 years (48) | 60 – 69 years (88) | ≥ 70 years (63) | Total 273  |
|--------------|-------------------|--------------------|--------------------|-----------------|------------|
| IFG alone    | (0) 0             | (0) 0              | (1) 1.1            | (16) 25.4       | (17) 6.2   |
| IGT alone    | (18) 24.3         | (4) 8.3            | (6) 6.8            | (1) 1.6         | (29) 10.6  |
| IFG + IGT    | (2) 2.7           | (1) 2.0            | (0) 0              | (0) 0           | (3) 1.1    |
| Pre-diabetes | (20) 27.0         | (5) 10.4           | (7) 7.9            | (17) 27         | (49) 17.9  |
| URDM         | (0) 0             | (5) 10.4           | (7) 7.9            | (0) 0           | (12) 4.4   |
| NGT          | (54) 72.9         | (38) 79.1          | (74) 84.1          | (46) 73.0       | (212) 77.6 |

**Table 4: Prevalence (%) of IFG, IGT, IFG + IGT, URDM and NGT in the female population and variation with age; number in bracket.**

| Condition    | 40 – 49 Year (226) | 50 – 59 years (323) | 60 – 69 years (172) | ≥ 70 years (18) | Total 739  |
|--------------|--------------------|---------------------|---------------------|-----------------|------------|
| IFG alone    | (27) 11.9          | (2) 0.6             | (1) 0.6             | (16) 88.9       | (46) 6.2   |
| IGT alone    | (5) 2.2            | (47) 14.5           | (17) 9.0            | (1) 5.5         | (70) 9.5   |
| IFG + IGT    | (3) 1.3            | (5) 1.5             | (0) 0               | (0) 0           | (8) 1.2    |
| Pre-diabetes | (35) 15.5          | (54) 16.7           | (18) 10.5           | (17) 94.4       | (124) 16.7 |
| URDM         | (7) 3.1            | (53) 16.4           | (15) 8.7%           | (0) 0           | (75) 10.1  |
| NGT          | (184) 81.4         | (216) 67            | (132) 76.7          | (1) 5.5         | (533) 72.2 |

## DISCUSSIONS

The prevalence of pre-diabetes in the study population was high. This underscores the need for routine screening for this condition to prevent development of diabetes.

There is no ready explanation for the prevalence curve for PD declining in the 5<sup>th</sup> and rising to a peak in the 7<sup>th</sup> decade of life. However, since URDM was most prevalent in the preceding decade (4<sup>th</sup>), it could be surmised that the decline was due to progression to diabetes. The prevalence of URDM and PD before the 7<sup>th</sup> decade was mostly due to IGT and this agrees with the assertion that IGT is better predictor of future DM than IFG,<sup>[4]</sup> and that IGT may be directly involved in the pathogenesis of cardio-vascular disease (CVD) and has a higher risk for CVD than IFG.<sup>[7]</sup> Earlier in life, PD may be more certainly detected using OGTT/2hppG than FPG alone.

The relationship between IGT and URDM may be due to the fact that in IGT, there are decreased early-phase (01-10min) and late-phase (60 – 120min) post-prandial insulin secretion. The defective late phase insulin secretion, combined with muscle and hepatic insulin resistance also present in IGT, results in prolonged hyperglycemia after a glucose load. In IFG, there is decreased early-phase but normal later-phase insulin

secretion combined with only hepatic insulin resistance.<sup>[18]</sup> Diabetes can more easily develop from IGT than IFG. IGT is also a leading cause of end-stage renal disease and of blindness with a high risk for neuropathy and gangrene,<sup>[19]</sup> It has a potentially important role in public health and as target for experimental strategies for prevention of type 2 diabetes.<sup>[4]</sup> Individuals with IGT may be euglycaemic in their daily lives as shown by normal glycated haemoglobin. They manifest glucose intolerance only when challenged with an oral glucose load. FPG may suffice for diagnosis PD in the 70s and beyond but not earlier than that.

Most of the IFG seen in this study occurred in the 7<sup>th</sup> decade of life when no case of URDM was detected. It had been noted that both FPG and 2hppG increases with age.<sup>[20]</sup> In the elderly women it was said to be due to higher rate of meal appearance and lower rate of glucose disappearance immediately after meal. In the elderly men it was said to be due decreased rate of glucose disappearance.<sup>[20]</sup> From this study it may not be desirable to screen for DM in subject aged ≥ 70 years even though they are likely to manifest IFG.

Peak values for BMI and WHR coincided with that of IGT in the population and this may account for the high prevalence of IGT in this 5<sup>th</sup> decade of life. Obesity,

especially visceral obesity, is associated with insulin resistance. More men than women had IGT, 10.6%, 9.5% respectively and IFG was detected in the same percentage of males and females, 6.2%. This is not in agreement with the report of Blaak, (2008) who reported higher prevalence of IGT in women than men and vice versa.<sup>[21]</sup>

Baseline glucose is the most consistent predictor of progression to diabetes. Plasma glucose was elevated in the 4<sup>th</sup> and 5<sup>th</sup> decades of life falling in the next decade, 60 – 69 age range and this is found to be the case in this study. The rise in plasma glucose in the  $\geq 70$  years range results from IFG with low probability of development of diabetes mellitus as seen in this study. IFG developed in the female subjects much earlier in life, 40 – 49 years, than in the male subjects  $\geq 70$  years. The females also had an increased prevalence of IFG in  $\geq 70$  years age range. Glucose metabolism in the females is affected by the menstrual phase when the energy demand is high due to suppression effect of oestrogens and progesterone on gluconeogenesis.<sup>[22]</sup> There were significant male-female differences in both FPG and 2hppG in this study contrary to the report of Basu *et al* (2006) 20 of no difference in 2hppG due to sex.

## CONCLUSIONS

Age, sex and weight affect glucose metabolism adversely. IGT is a better predictor of future diabetes than IFG and the 5<sup>th</sup> decade of life is most crucial in the progression of PD to diabetes. In the male group, pre-diabetes was common in the 4<sup>th</sup> and 7<sup>th</sup> decade while in the female group prevalence was more evenly distributed though the years. After the 6<sup>th</sup> decade of life, progression of PD to URDM seems to cease. Screening for glucose metabolic disorders is better done using OGTT/2hppG than FPG. The report showed high prevalence of glucose intolerance and un-reported diabetes mellitus in the population. The need for regular screening of the population for glucose intolerance was highlighted in order to reduce the incidence of diabetes and its complications.

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