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# Experience with Common Anti-hypertensives Regarding Development of Impaired Glycaemia in a Specialised Primary Care Facility in Jos, Nigeria

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**Abstract:** Hypertension (HBP) and diabetes (DM) co-exist with worse outcomes. Various hypotheses explain this, one of which is the drug used to treat HBP. One therefore sought to see what drug (s) have this potential and under what conditions they manifest. This is to guide future practice, and reduce morbidity. Consequently, hypertensives attending this specialized primary care facility who had no diabetes, recent ischaemic phenomenon and not in heart failure were studied with blood glucose as outcome measure. Basic clinico-demographic data and information related to the HBP were collected. A total of 210 hypertensives seen over the study period satisfied enrolment criteria; out of whom 108 were females. Mean age was 56.42 (10.46) with a span of 31 to 88 years. Most of them were middle aged. HBP history ranged from 5 to 240 months; with a mean of 71.74 (53.35). Their mean (SD) FBG when first seen in the clinic was 5.10 mmol/l (0.94) which marginally rose to 5.20 mmol/l (0.85) by the time of the study. The glucose was more likely to rise in females (p=0.013), with longstanding HBP (p=0.000), use of beta blockers/diuretic (p=0.014), co-administration of statins (p=0.006) and with metabolic syndrome co-morbidity (p=0.028). In conclusion, chances of developing impaired glycaemia or new onset DM with antihypertensive treatment are higher in women, family history of diabetes, longer duration of hypertension, use of beta blockers or thiazide diuretics, use of statins and presence of the metabolic syndrome. These should be considered while initiating treatment in hypertensives to avoid introducing additional risk factors.

**Keywords:** Diabetes, Onset, Treatment, Hypertension, Nigerian-African

## 1. Introduction

Most patients with systemic arterial hypertension develop impaired glycaemic control or frank diabetes mellitus (DM) with time [1]. At times it is thought to result from the type of drug deployed [2] or time dependent effects of co-morbidities like obesity which such patients invariably have. What is not known is whether the patients have DM latent in their genes [3], and may still have developed it with time, even if they did not develop hypertension earlier. It may also result from predisposing factors that such patients acquire with time. By whatever mechanism, both hypertension and DM lead to worse cardiovascular effects than either alone. It is for this reason that the United States Preventive Services task Force recommended the screening of hypertensives for diabetes in 2008 [4]. If the grave statistics of morbidity and survival are to be mitigated, efforts to ensure that one does not develop on the other [1] should be intensified.

One therefore in a group of hypertensives accessing care in this specialized hypertension primary care facility sought to see what factors predisposed them to develop abnormal glucose profile with antihypertensive treatment. Any such factor will be taken into consideration in future practice to ameliorate the effects of this double jeopardy.

## 2. Methods

In this private specialized primary care centre, patients come on self-referral largely or on recommendations by doctors and relations for cardiovascular care. Most of them

however are hypertensives. Clientele cuts across age, gender, ethnicity, social class and religion. Appointment cycle is between 2 weeks and 3 months; so this study lasted for 3 months between October and December 2016.

Once seen in the study, patients were not considered again even if they were given appointments in between the study period. The focus was on patients who were following up solely for hypertension with no associated DM or heart failure. The only complications that did not serve as exclusion criteria were stroke and myocardial infarction if they were more than 6 months in duration. On enrolment, the involvement was explained to them and their consent sought. They all willingly gave permission since it was largely information from their records; and according to them, they dreaded developing diabetes on the on-going hypertension. A data collection form was designed and used by the author. Information of interest were: age, gender, fasting blood glucose (FBG) on that occasion, drugs in use, duration of hypertension since diagnosis, weight on date of enrolment (measured with a bathroom scale set at zero for each patient), family history of DM, whether chronotherapy was applied to treatment and remarks which dwelt on presence of metabolic syndrome or statin co-administration. They were then requested to repeat FBG that they presented on their next visits. FBG was estimated after an overnight fast.

Statistics: Data were analysed in the Computer Centre of University of Jos using SPSS version 22. Quantitative data are presented as means (SD); and t test used to determine group differences. Qualitative data are presented as proportions. One way ANOVA was used to compare means between groups; and post-hoc tests for multiple comparisons. Significance was set at $p < 0.05$.

# 3. Results

A total of 210 hypertensives seen over the 3 month period satisfied the criteria for enrolment; out of whom 108 were females. Their ages ranged from 31 to 88 years with a mean (SD) of 56.42 years (10.46). Most of the patients were in the 55 to 64 year bracket. They had been hypertensive for periods ranging from 5 to 240 months; with a mean (SD) of 71.74 months (53.35). Their mean (SD) FBG when first seen in the clinic was 5.10 mmol/l (0.94) which marginally rose to 5.20 mmol/l (0.85) by the time of the study.

With blood glucose as an outcome measure, ANOVA was done to determine difference between groups for gender, family history and chronotherapy. The difference between means was significantly higher in favour of females at p=0.013. Presence of family history of DM and use of chronotherapy in drug administration were not statistically significant; though for the former there was a tendency for a rise in mean FBG.

With weight divided into 3 categories: less than or equal to 75 kg, 75 to 99 kg and greater than or equal to 100 kg, there was no significant difference in blood sugar along the line of categorization. For age also divided into 3 categories: < 45 years, 45-64 years and > 65 years, there was no significant difference in blood sugar.

Duration was however relevant as the between group difference in sugar rose with duration of hypertension and attained statistical significance (p=0.000). In relation to drugs, the rise in sugar where significant was only when "culprit" antihypertensive drugs (beta blockers and or thiazide diuretics) [5, 6] were used (p=0.014). Where these drugs were given together with "non-culprit" drugs, or "non-culprit" drugs alone, the differences were not statistically significant. Use of statins also caused a significant rise in blood glucose (p=0.006) as well as presence of metabolic syndrome (p=0.028).

# 4. Discussion

Hypertension co-existing with impaired glycaemic control, either as such or as part of the metabolic syndrome worsens cardiovascular outcome [7]. There is therefore the need to prevent development of either diabetes or metabolic syndrome on hypertension; as studies have shown that rising glucose levels in the course of antihypertensive therapy leads to future cardiovascular morbi-mortality [8].

In this study, the author had tried to look for situations that make for worsening glycaemic control in hypertensive patients on follow-up in his specialized hypertension primary care facility. Women were more likely than males to develop impaired glycaemia with time, on antihypertensive treatment [9]. This could be explained variously. They tend to have metabolic syndrome more than males [10, 11]; and when treated with statins in this condition have a greater risk of developing new onset diabetes mellitus [12]. Again, they handle drugs differently compared to men. One of the ways by which antihypertensives influence glucose metabolism is by influencing blood flow to skeletal muscles and the liver. Improved flow implies better disposal of blood glucose. This is better in men, and so when exposed to such drugs men would clear blood sugar better. This leaves women with the burden of hyperglycaemia [13].

Hypertensives who had a family history of diabetes mellitus tended to develop diabetes with time, though statistically significant difference was not attained. It may have required a larger sample size or a longer duration to manifest. Development of DM with antihypertensive therapy is known to be more likely when risk of DM is high, as in individuals with family history of DM [14]. Though application of chronotherapy is known to result in reduction of risk for DM if drugs are given at bed time [15], this effect is more for blockers of renin angiotensin aldosterone system and did not emerge in our study. It is not exactly certain why this was the case here. It may require a fresh study directly interrogating for this for the expected result to become evident. Weight and age made no difference between and within groups. The association where it exists tends to decline with body mass index and age [1]; and may explain the finding in this study.

The tendency for blood sugar to rise with duration of treatment attained statistical significance at the level of p=0.000. Yearly incidence of new onset diabetes in a study as reported by Verdecchia et al [15] confirms this experience.

This stands to reason as time sustains whatever adverse effect to glucose metabolism there may be in relation to drugs. Also with time, patients get older and age is a risk factor for new onset diabetes; as insulin secretion wanes with age and associated physical inactivity. Prevalence of metabolic syndrome equally rises [16].

Use of what was called "culprit drugs", diuretics and beta-blockers was related to a rise in blood sugar with time. Several workers have documented this in the past [17, 18]; the explanation being drug effects on peripheral blood flow, insulin receptors, liver and insulin release. When peripheral blood flow to skeletal muscles is good, glucose disposal to the tissues is facilitated. Drugs like beta blockers do not increase peripheral blood flow except the cardio-selective vasodilatory ones [19]. For thiazides, it is related to the promotion of hepatic insulin resistance and impaired insulin release by the beta pancreatic cells provoked by the hypokalaemia that they cause [20]. Interestingly this manifestation was if these drugs were used alone. When combined with drugs from other classes, this effect was suppressed. Statins used as part of treatment of these patients in the presence of dyslipidaemia resulted significantly to the development of impaired glycaemia. This aligns with the study of Shen et al [21] where they posited that in people at risk of impaired glycaemia, diuretic and statin use is likely to result in new onset diabetes mellitus. Statins on their own have been suggested to directly decrease synthesis and secretion of insulin thereby exacerbating insulin resistance [22].

That the tendency to develop impaired glycaemia was more in patients with metabolic syndrome is not surprising. Metabolic syndrome is a constellation of risk factors with android obesity as the flagship. In obese patients, the adipocytes are metabolically active and release non-esterified fatty acids, glycerol, hormones and pro-inflammatory cytokines. These result in insulin resistance. Over time, pancreatic beta cells become dysfunctional; resulting in dysglycaemia and diabetes mellitus [23].

The weakness of this study is in being a solitary primary care private facility experience with relatively small sample size. External validity thus becomes a concern. Its strength however derives from being undertaken in a specialist practice where cases with such bearing are concentrated. The duration of follow up was also reasonable and gave time for any impairment of glycaemia to develop. Again and more importantly, each patient served as his or her own control.

# 5. Conclusion

Chances of developing impaired glycaemia or frank new onset diabetes mellitus with antihypertensive treatment are higher in women. Family history of diabetes, longer duration of hypertension, use of beta blockers or thiazide diuretics alone, use of statins and presence of the metabolic syndrome all go to increase the tendency to develop impaired glycaemia in hypertensives. They should be considered while initiating treatment in hypertensives to avert the double jeopardy which worsens cardiovascular morbi-mortality.

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# Conflict of Interest

The author declares that there is no conflict of interest.

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