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Co-Existent Hypertension with Diabetes Mellitus Exacerbates Renal Dysfunctions

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Abstract

Hypertension as well as diabetes mellitus has been reported to be a major risk factor for deteriorating kidney functions. However, there is paucity of reports on renal functions in a co-existence of hypertension and diabetic condition, hence, this study evaluates renal functions in hypertensive and diabetic co-morbidity. Participants were categorised into healthy, hypertension, diabetes and hypertension with diabetes group. Blood pressure was measured as well as fasting blood glucose and blood samples were collected from each participant to assay renal function indices. The results showed that there was substantial uraemia as well as a significant reduction glomerular filtration rate in co-morbid hypertension and diabetic patients. Fasting blood glucose and mean arterial blood pressure were considerably elevated while creatinine concentration was not significantly altered in comorbid hypertension and diabetic patients. This study revealed that co-existence of hypertension and diabetes mellitus exacerbated renal dysfunction comparatively to hypertension and diabetes mellitus.

Keywords: Hypertension; Diabetes mellitus; Renal functions; co-morbidity; Uraemia.

INTRODUCTION

As part of the metabolic syndrome, diabetes mellitus (DM) is characterized by hyperglycemia and/or glucose intolerance as a result of inadequate insulin production, improper insulin action, or both (Galicia-Garcia *et al.,* 2020). An important factor in the pathogenesis of this disease has been reported to be dysregulations in the regulatory systems for storage and mobilization of metabolic fuels including the catabolism and anabolism of carbohydrates, lipids, and proteins resulting from defective insulin secretion, insulin action, or both (Gonzalez-Gil and Elizondo-Montemayor 2020). Multiple organ failures and increasing metabolic problems such as retinopathy, nephropathy, and/or neuropathy are among the severe symptoms of DM (Preguiça *et al.,* 2020). About 171 million individuals worldwide have been diagnosed with DM and its frequency is rising quickly, especially in developed nations (Cao *et al.*, 2020). The World Health Organization (WHO) predicted that by 2030, the number would have doubled (WHO, 2006). Urbanization and lifestyle changes have been blamed for the rise in diabetes cases in emerging nations, although the processes are still poorly understood (Akdis, 2021). It was discovered in a follow-up cross-sectional study of people with diabetes in Rivers state (the central part of the Niger Delta region) that diabetes significantly contributes to the health issue with type 2 diabetics presenting upon diagnosis (Maiga *et al.*, 2020).

Several cardiovascular problems including hypertension, vasculopathy, and congestive heart failure (CHF) have been related to diabetes mellitus by a body of research evidence. A chronic medical disorder known as hypertension (HTN) is caused by sustained high blood pressure in the arteries (Gupta *et al.,* 2021). Usually, high blood pressure has no symptoms. However, persistently high blood pressure is a significant risk factor for dementia, atrial fibrillation, peripheral vascular disease, vision loss, chronic renal disease, heart failure and coronary artery disease (Panula *et al.,* 2020). Systolic and diastolic pressures; the highest and lowest lateral pressures applied to the arterial wall respectively are the two parameters used in clinical blood pressure measurements. Most persons' typical resting blood pressure falls within the ranges of 60-80 mmHg diastolic and 100-130 mmHg systolic (Balwan and Kour, 2021). The majority of persons have high blood pressure if their resting blood pressure is consistently 130/80 or 140/90 mmHg or higher (Balwan and Kour, 2021). Children are subject to different numbers (Balwan and Kour, 2021). Numerous patients have been reported to have both diabetes mellitus and hypertension. Nigerians have both diabetes and

hypertension rates of 10 to 15% and 1 to 2% respectively (Edeogu *et al.,* 2020). Most cases of hypertension in people with type 2 diabetes are caused by essential hypertension (Akalu and Belsti, 2020). According to studies, patients with diabetes experience hypertension two times more frequently than people without the condition (Asiwe *et al.,* 2021a). Hypertension is strongly and independently correlated with diabetes incidence (Palaiodimos *et al.,* 2020). Elevated blood pressure makes diabetic individuals more susceptible to problems such cardiovascular disease, stroke, renal disease, and retinopathy (Cardoso *et al.,* 2020). The kidney is a crucial organ for homeostasis and has been linked to both diabetes and hypertension (Tinti *et al.,* 2021). Chronic kidney disease is frequently detected after an examination of those thought to be at risk for renal problems such as those with high blood pressure and/or diabetes because the symptoms of failing kidney functions are not always clear (Asiwe et al 2021b). There are not many researches looking into the connection between diabetes, hypertension, and the onset of renal failure. Recent investigations on patients with type 1 and type II diabetes found a link between dietary salt consumption and diabetic complications (Asiwe *et al.,* 2021a). To the best of our knowledge, however, there is a dearth of information in the literature about the kidney's functionality in a condition where diabetes and hypertension are coexisting. As a result, the goal of this current study was to evaluate renal functions in co-morbid state of hypertension and diabetes.

MATERIALS AND PROCEDURES

Ethical Consideration

Before starting the study, a formal approval was received from the University of Benin Teaching Hospital's (UBTH) Ethics and Research Committee (ADM/E22/A/VOL.VII/148283) which adhered strictly to the National guideline for research and experimentation (NIH Publication No. 85-23).

Criteria for Inclusion and Exclusion

The study excluded participants who are diagnosed within the last three years as well as those who are type I diabetes and also those with other health complications that might add bias to our study

Study Plan

A total of 100 willing participants who met the inclusion criteria were recruited for the cross-sectional analytical study from the diabetes and hypertension clinic, Out-patient Department (OPD) of University of Benin Teaching Hospital (UBTH), Benin, Nigeria. They were divided into four groups, each with 25 participants (n=25), consisting of healthy individuals (controls), hypertensive patients (HTN), diabetes mellitus patients (DM), and patients with both hypertension and diabetes mellitus (HTN/DM).

Sample Collection

Consented participants were given a set of structured questionnaire in order to get information on their medical history. The blood pressure of the participants was measured using a sphygmomanometer and weight was measure using a weighing scale. The blood samples gotten from the participant were drawn into 5ml EDTA bottle for fasting blood glucose level check and thereafter centrifuged at 3000 rpm for 5 minutes and the plasma decanted for other assays such as urea and creatinine test. This procedure was carried out early in the morning when the participants had not had their breakfast.

Measurement of Plasma Creatinine

The alkaline Jaffe's Picrate assay was used to measure the plasma creatinine level (Owen *et al.,* 1954). The Jaffe's method for measuring blood creatinine is based on the idea that when creatinine combines with picric acid in an alkaline media, an orange-colored complex with the alkaline picrate is formed. At 490nm, a spectrophotomer measures the complex's absorbance, whose strength is directly proportional to the amount of creatinine present in the sample.

Plasma Urea Level Determination

According to Cheesbrough (2005), the plasma urea level was measured using the diacetylmonoxime technique. The diacetylmonoxime method produces a reddish solution whose absorbance is measured at 530nm in a spectrophotomer by reacting urea with diacetylmonoxime at high temperature in an acid medium in the presence of cadmium ions and thiosemicarbazide.

Calculated Creatinine Clearance Determination

Using the Cockcroft-Gault formula, the creatinine clearance, which is nearly identical to the glomerular filtration rate, was calculated (Cockcroft and Gault, 1976). Since plasma creatinine is so strongly influenced by age, sex, and body size, the method takes into account a number of variables that have an impact on the estimation of muscle mass and assumed creatinine generation. Creatinine clearance is expressed as follows: Creatinine clearance (mol/L) = (140 - age) x weight)/ (0.814 x plasma [creatinine]) x (0.85 if patient is female), where creatinine clearance is expressed in milliliters per minute age is expressed in years, weight is expressed in kilograms, and [creatinine] is expressed in micromoles per liter.

Statistical Analysis

The results were statistically evaluated using Graphpad prism version 8. Mean and standard error of the mean

were used to express the results. One way analysis of variance (ANOVA) and Tukey post *hoc* test were used to check the data for any significant differences. At $p<0.05$, mean variation was considered significant.

RESULTS

Co-morbidity of hypertension and diabetes mellitus has been reported to be a major risk factor for deteriorating kidney functions. Following one-way analysis of variance (ANOVA) and student t-test, we evaluated the renal function indices in patients with hypertension (HTN), Diabetes mellitus (DM) and co-morbid condition of hypertension and diabetes (HTN/DM). There was a significant ($p<0.05$) elevation of plasma Urea [F(3,96)=4.45, $p=0.0057$] in DM and HTN/DM group comparatively to control **(Fig. 4)**. Also, in HTN/DM group, there was a significant ($p<0.05$) reduction in eGFR [F(3,96)=3.08, $p=0.0311$] comparatively to control **(Fig. 5)**. However, plasma concentration of Creatinine [F(3,96)=0.537, $p=0.6580$] was not significantly ($p>0.05$) altered in any of the groups when compared with control **(Fig. 3)**. Diabetes mellitus and hypertension was confirmed with a significant ($p<0.05$) elevation in fasting blood glucose (FBS) [F(3,96)=13.3, $p<0.0001$] and Mean arterial blood pressure (MAP) [F(3,96)=8.48, $p<0.0001$] in DM and HTN/DM as well as HTN, DM and HTN/DM respectively when compared to control as shown in **figure 1** and **Figure 2.**

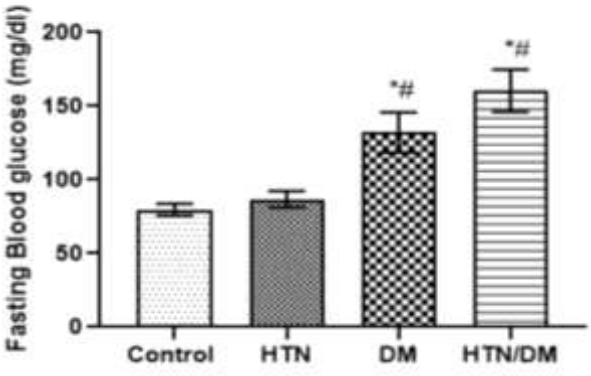

Figure 1. Fasting blood glucose. Values are represented as Mean ±SEM, n=25 and *p<0.05 was significant when compared to control while #p<0.05 was significant when compared to hypertension group. HTN=hypertension, DM=Diabetes mellitus and HTN/DM hypertension and Diabetes co-morbidity.

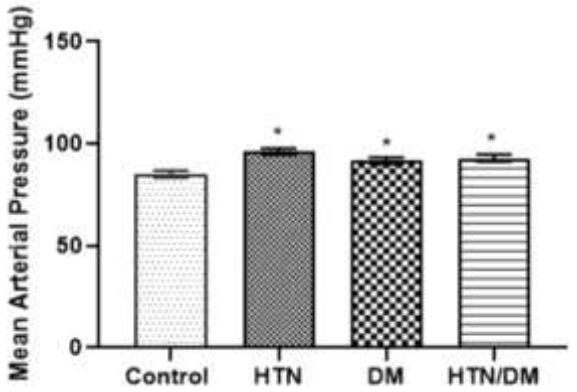

Figure 2. Mean Arterial Blood Pressure (MAP). Values are represented as Mean ± SEM, n=25 and *$p<0.05$ was significant when compared to control. HTN=hypertension, DM=Diabetes mellitus and HTN/DM hypertension and Diabetes co-morbidity.

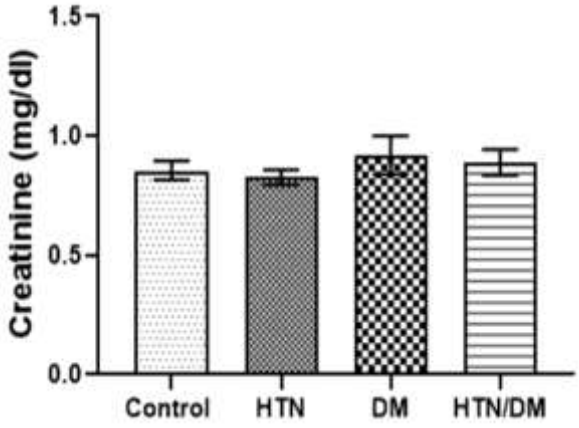

Figure 3. Plasma Creatinine concentration. Values are represented as Mean ± SEM, n=25 and *$p>0.05$ was not significant when compared to control. HTN=hypertension, DM=Diabetes mellitus and HTN/DM hypertension and Diabetes co-morbidity.

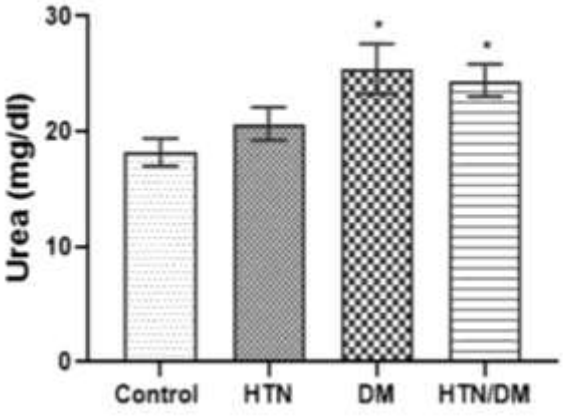

Figure 4. Plasma Urea concentration. Values are represented as Mean ± SEM, n=25 and *$p<0.05$ was significant when compared to control. HTN=hypertension, DM=Diabetes mellitus and HTN/DM hypertension and Diabetes co-morbidity.

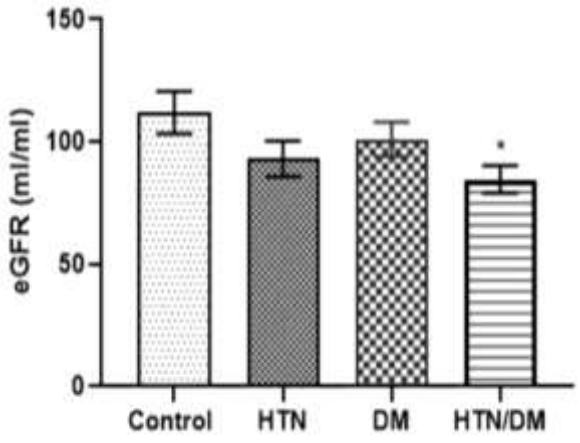

Figure 5. Estimated Glomerular Filtration Rate (eGFR). Values are represented as Mean ± SEM, n=25 and *$p<0.05$* was significant when compared to control. HTN=hypertension, DM=Diabetes mellitus and HTN/DM hypertension and Diabetes co-morbidity.

DISCUSSION

There are no specific signs or symptoms of deteriorating kidney functions, however they could include feeling generally unwell and losing appetite. Diabetes mellitus has long been known to negatively impact blood pressure, cardiovascular risk and survival. People who are known to be at risk of kidney issues, such as those with high blood pressure and diabetes mellitus, are frequently examined in order to diagnose chronic kidney disease (Byrne and Targher 2020). This study was conducted to assess renal function in patients with diabetes and hypertension as well as a co-morbid condition of hypertension and diabetes. In this study, patients with diabetes as well as hypertension and diabetes had substantial uraemia. Additionally, it was found that diabetic and hypertensive (HTN/DM) patient's eGFR dramatically decreased as compared to healthy patients (control group). However, none of the patients' creatinine levels were considerably changed. The possibilities of having renal problem and other complications that involves organ dysfunction increases significantly when diabetes mellitus and hypertension are co-diagnosed. This is especially true if the underlying illnesses are left untreated. Deteriorating kidney functions are most frequently caused by diabetes in Nigeria (Okaka *et al.,* 2020; Ibitoba *et al.,* 2022). Diabetic and hypertensive patients also have increased prevalence of cardiovascular (CV) risk factors, such as dyslipidemia, microalbuminuria, hyperuricemia, a propensity to clot, and left ventricular hypertrophy (Mantovani *et al.,* 2020; Sanusi *et al.,* 2020; Okonofua *et al.,* 2021).

We reported an elevated mean arterial blood pressure in diabetic patients (fig.2) which was consistent with previous reports that vascular consequences of diabetes includes renal disease, coronary heart disease, stroke, peripheral vascular disease, lower extremity amputations as well as retinopathy and these are exacerbated by hypertension (Asiwe *et al.,* 2021b). Furthermore, our research showed that individuals with both diabetes and hypertension have a 5- to 6-fold increased risk of developing renal failure compared to individuals with hypertension alone and no sign of diabetes (fig. 5). Although renal failure is a significant consequence for people with diabetes and hypertension, however, cardiovascular disease events account for the majority of deaths (Copur *et al.,* 2021). Renal failure caused by diabetes and hypertension is becoming more common despite improved knowledge and suggestions for preventive measures put out by many public health organizations. In Nigeria, the number of people beginning dialysis has steadily increased over the past 15 years mostly due to diabetes. This could be explained in part by a decrease in CV mortality which has led to a rise in the number of people living long enough to experience deteriorating kidney functions. A second, possibly more significant problem is that patients themselves may not be adhering to prescribed drug regimens as well as caregivers not been adequately able to educate the patients. As a result of these, target blood pressure goals are not met which increases the likelihood of developing renal failure. The general population's rates of controlling hypertension have dropped recently, according to data from the third National Health and Nutrition Examination Survey (NHANES III) (Zheutlin *et al.,* 2022). The prevalence of diabetes has continued to climb which is a third factor that contributes to the rising incidence of renal failure (Cheng *et al.,* 2020). Last but not least, the rise in CV and subsequent renal morbidity in recent years has also been influenced by the rising frequency of heart failure; as a result, even while mortality related to hypertension has declined, morbidity has grown. Diabetes often results in hypertension, especially when nephropathy is also present. About 85% of persons with type 2 diabetes mellitus that have nephropathy before needing dialysis or a kidney transplant also have hypertension, which is roughly twice as common in those with type 2 diabetes as in those without it (Asiwe *et al.,* 2021). Renal failure can be a third limb of a tripod-stand disease condition of hypertension and diabetes because of their common path-biological etiologies. However, to prevent or treat one, the others must be taken into consideration to reduce mortality.

CONCLUSION

The results of our study reveal that diabetes and hypertension are risk factors for developing renal failure and also hypertension and diabetic co-morbidity exacerbated the deteriorating kidney functions by

significantly reducing glomerular filtration rate and increasing plasma urea concentration. However, it is therefore recommended that awareness and enlightenment programs should be encouraged to educate diabetic patients as well as hypertensive patients the need to take their medications serious to avoid renal function complications.

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Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical consideration: The approval for this study was granted by the University of Benin Teaching Hospital's (UBTH) Ethics and Research Committee with approval number ADM/E22/A/VOL.VII/148283.

Consent to Participate: participants willingly consented to participate in this study by filling and submitting a written consent form to the authors.

Consent to Publish: All authors approved the submission and publication of this manuscript.

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