The Impact of Co-existence of Diabetes and Hypertension on Oxidative Stress in non Obese Subjects

Idonije O. Blessing and Onigbinde O. Abraham

Co-occurrence of diabetes and hypertension is not unfamiliar in the world today and where this co-exists, it is said to aggravate cardiovascular complications. On the other hand, the significance of oxidative stress in cardiovascular condition has been recognized. Hence, this study investigated the impact hypertension and diabetes mellitus has on oxidative stress and the status of some antioxidants in non obese subjects. The study involves 204 non obese subjects who are hypertensive (NOH; n = 53), diabetes (NOD; n = 51), diabetes and hypertensive (NODH; n = 40) and non hypertensive non diabetes (NONDH; control; n = 60). There ages, blood pressure, fasting blood glucose and body mass index were determined using standard techniques while their oxidative stress and antioxidants status were analyzed via standard laboratory procedures. The results showed no significant difference in the ages and BMI in the entire groups. However, blood pressure was significant higher in the hypertensive groups while fasting blood glucose was higher in the diabetes group compared with the control. Oxidative stress was significantly higher (p<0.05) in the NOD, NOH and NODH groups compared to the control group (NONDH; 5.32±1.85). Compared to the NONDH group, vitamin A was not significantly different (p>0.05) between the groups, vitamin E was significantly higher in group NODH (13.58±5.28) and nitric oxide was significantly lower (p<0.05) in the NOH (30.87±3.48) and NODH (30.30±3.13) groups. Judging by the findings of this study, hypertension and diabetes, either existing alone or in combination have a negative impact on oxidative stress and antioxidant status.

Key words: Hypertension, diabetes, co-existence, non obese
INTRODUCTION

Diabetic patients have been shown to have increased prevalence of hypertension compared to the general populace (Cowie and Harris, 1995; Anonymous, 1993; Kannel and McGee, 1979). However, patients with co-morbid conditions usually present with one first before the other(s) is/are diagnosed or simultaneously they can co-present and be diagnosed. According to Gress et al. (2000), hypertension and diabetes mellitus are independent risk factors for Cardiovascular Diseases (CVD) thereby increasing morbidity and mortality where they co-exist.

It has been reported that hypertension in diabetes accelerates the development and progression of microvascular and macrovascular complications in patients with diabetes (Adler et al., 2000). This is also true in diabetic Nigerians who showed increased mortality with development of hypertension as compared with normotensive diabetic Nigerians (Kolawole and Ajayi, 2000; Ngwogu et al., 2012).

The study of the biochemistry of free radicals has increased since the realization that many major human diseases may involve, in their aetiology, free radical processes and that antioxidant therapy may delay or prevent these processes. Free radicals have been implicated as a contributing factor to the pathophysiology of major chronic diseases such as heart disease and cancer (Halliwell and Gutteridge, 1989; Halliwell et al., 1992). The pathological role of oxidative stress in vascular diseases is well recognized (Madamanchi et al., 2005). Could this be a suggestion that the antioxidants regulatory mechanisms that check oxidative processes are troubled by hypertension and diabetes? Considering the increasing rate of these diseases in the general population and the burden they have on the world economic, it become necessary to investigate what the antioxidants strength and oxidative stress status might be in such conditions as this may provide a clue to their management.

The objective of the study therefore, was to investigate the impact hypertension and diabetes has on oxidative stress and the status of some antioxidants in non obese subjects.

MATERIALS AND METHODS

Study area: This study was conducted in Ekpoma, Benin City, Kwale and Asaba, all in the south-south zone of Nigeria.

Study design: This study is a cross-sectional study involving simple random sampling and cohort sampling for subjects recruitment.

Ethical consideration: Ethical approval was sought and given by the research and Ethic Committee of Ambrose Alli University, Ekpoma. The intervention and control community gave their permission after the aims and objectives of the study were explained to them. Also, informed consent was sought and obtained from the respondents before enrollment into the study. At the end of the study the control group was also given the same intervention, for ethical reasons. Written informed consent/questionnaire were administered to all subjects.

Sampling method and sample size: A simple random sampling was done to recruit subjects for the study. The sample size was determined as described as follows by this formula:

\[ N = \frac{pq}{\sum \frac{1}{q^2}} \]

Where:

- \( N \) = Sample size
- \( P \) = Population or Prevalence rate (50% or 0.5)
- \( q \) = 1 - 0.2
- Error margin = 0.05

Subjects and grouping: Subjects were classified into the following 4 groups to meet the set goals of this research. Group 1: Non Obese Diabetic (NOD), Group 2: Non Obese Hypertensive (NOH), Group 3: Non Obese Diabetic/Hypertensive (NODH), Group 4: Non Obese Non Diabetic/Hypertensive [normal control (C)].

They were classified as non-obese using BMI ≤ 24.5 kg m\(^{-2}\), diabetic using fasting plasma glucose (FBG) ≥ 7 mmol L\(^{-1}\) (126 mg dL\(^{-1}\)), hypertensive using blood pressure of ≥ 140/90 mmHg and a total of about two hundred and four subjects were recruited and distributed as follow:

- NOD = 51; NOH = 53; NODH = 40; NONDH = 60

Inclusion criteria: All subjects with BMI ≤ 24.5 kg m\(^{-2}\) and not on any form of medication were recruited.

Exclusion criteria: All subjects who are obese (BMI ≥ 24.5 kg m\(^{-2}\)) and non obese already diagnosed as been hypertensive and/or diabetic who are on medications were excluded from this study.

Blood pressure measurement: Resting blood pressure was taken in a sitting position after a 5-10 min rest using
RESULTS

Table 1 is the Mean±standard deviation of ages, blood pressure, fasting blood glucose levels and body mass index of the different groups in the sampled population. The NOH group showed a mean age of 51.34±11.88 years and was the oldest while those in NONDH group were the youngest with a mean age of 42.33±14.64 years. The entire groups were within the normal ranges of BMI (kg m\(^{-2}\)) with the NOH group (23.51±1.69 kg m\(^{-2}\)) presenting the lowest and the NONDH group (24.15±2.27 kg m\(^{-2}\)) presenting the highest. Statistically, there was no significant different in the ages and BMI of the sampled population between the groups. On blood pressure, the systolic and diastolic blood pressure of the NOH and NONDH groups were higher (168.20±17.74/98.13±9.81 and 163.50±21.44/97.73±11.43 mmHg, respectively) and these were significant (p<0.05) compared to the NONDH group (125.50±10.14/70.77±11.29 mmHg) and the NOD group (132.50±9.81/78.47±10.99 mmHg). On the other hand, fasting blood glucose was highest in the NONDH group (11.32±3.30), higher in the NOD group (11.04±3.30) and high in the NOH group (4.83±3.30) compared to the NONDH group (3.93±0.85). These differences in FBG were statistically significant (p<0.05) in the NOD, NOH and NONDH groups compared with the control.

Table 2 shows the level of oxidative stress in the studied population indicated via MDA status and antioxidant level. Compared to the control group (NONDH, 5.32±1.85), the NOD, NOH and NONDH groups showed significantly higher (p<0.05) MDA levels. On the antioxidant status, the level of vitamin A was not

<table>
<thead>
<tr>
<th>Parameter</th>
<th>NOD (n=51)</th>
<th>NOH (n=53)</th>
<th>NONDH (n=40)</th>
<th>NONDH (n=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE (years)</td>
<td>54.69±13.90</td>
<td>51.34±11.88</td>
<td>48.45±10.50</td>
<td>42.33±14.64</td>
</tr>
<tr>
<td>BMI (kg m(^{-2}))</td>
<td>23.75±2.70</td>
<td>23.51±1.69</td>
<td>24.15±2.27</td>
<td>23.62±2.030</td>
</tr>
<tr>
<td>BP systolic</td>
<td>132.50±9.81</td>
<td>168.20±17.74</td>
<td>163.50±21.44</td>
<td>125.50±10.14</td>
</tr>
<tr>
<td>BP diastolic</td>
<td>78.47±10.09</td>
<td>58.13±0.81</td>
<td>97.73±11.43</td>
<td>70.77±11.29</td>
</tr>
<tr>
<td>FSG (mmHg)</td>
<td>11.04±3.30</td>
<td>4.83±1.30</td>
<td>11.32±3.30</td>
<td>3.93±0.85</td>
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<tr>
<th>Parameter</th>
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<th>NONDH (n=60)</th>
</tr>
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<tbody>
<tr>
<td>MDA</td>
<td>6.49±1.51*</td>
<td>6.28±1.72*</td>
<td>6.86±1.70*</td>
<td>5.32±1.85</td>
</tr>
<tr>
<td>Vit. A</td>
<td>0.45±0.22</td>
<td>0.47±0.26</td>
<td>0.42±0.21</td>
<td>0.45±0.23</td>
</tr>
<tr>
<td>Vit. E</td>
<td>13.41±5.28*</td>
<td>11.86±5.47</td>
<td>13.58±5.28*</td>
<td>11.66±4.27</td>
</tr>
<tr>
<td>NO</td>
<td>31.04±2.82</td>
<td>30.87±3.48</td>
<td>30.30±3.13*</td>
<td>32.37±2.53*</td>
</tr>
</tbody>
</table>

*Significantly different at p<0.05 from the control (NONDH)
significantly different (p>0.05) between the groups. However, vitamin E was significantly higher in NODH group (13.58±5.28) compared to the NONDH group (11.66±4.27) and others. In addition, the value of nitric oxide was significantly lower (p<0.05) in the NOH (30.75±3.48) and NODH (30.30±3.13) groups compared to the NONDH (32.37±2.53) and the NOD (31.04±2.82) groups.

**DISCUSSION**

The present study indicated that diabetes and hypertension potentiate oxidative stress and where they co-exist, oxidative stress is severely aggravated. In addition, according to the present results, diabetes has more potential in worsening oxidative stress compared to hypertension. In accordance with the present finding, increase in oxidative stress has been reported in human hypertension (Kashyap et al., 2005; Sun et al., 2006; Lip et al., 2003) and diabetes (Maddux et al., 2001; Rudich et al., 1998; Matsuoka et al., 1997) and these were based on increased levels of biomarkers of lipid peroxidation and oxidative stress.

Although, studies have reported oxidative stress to play critical roles in the pathogenesis of many diseases (Brownlee, 2001), the suggestion that it impair insulin secretion by pancreatic β cells (Matsuoka et al., 1997) and glucose transport in muscle (Maddux et al., 2001) may explained the finding in the NOH and NODH groups. Extended exposure to high levels of Reactive Oxygen Species (ROS) can damage DNA, proteins and lipids (Bate, 2004). Hence, long term diabetes and hypertensive exposure may be more detrimental to health. In line with this assertion, increased oxidative stress in vascular walls has been shown to be involved in the pathogenesis of hypertension (Nakazono et al., 1991), atherosclerosis (Ohara et al., 1993) and hepatic steatosis (Roskams et al., 2003) and this may explained the contribution by the NOH and NODH groups. Putting together these information by Matsuoka et al. (1997), Maddux et al. (2001), Nakazono et al. (1991), Ohara et al. (1993) and Roskams et al. (2003), one cannot but support the aggravated MDA level in co-existence of diabetes and hypertension as showed by the NODH group. Indeed, it has been previously shown by studies that the co-existence of the two conditions is a powerful promoter of CVD, accelerating microvascular and macrovascular complications and greatly increasing cardiovascular stroke and end stage renal disease risk (Sowers, 2004; Sampanis and Zamboulis, 2008).

In terms of antioxidant status, the present study showed that the level of vitamin A was not significantly influence by diabetes and or hypertension, the level of vitamin E and nitric oxide were affected by the presence of diabetes and hypertension and this effect was severe where they co-exist. This finding is in line with previous reports (Kashyap et al., 2005; Sun et al., 2006) that vascular diseases lower antioxidants capacity judging by the significant reduction in nitric oxide level which is recognized as a potent inhibitor of the lipid peroxidation. In agreement with this, hypertensive condition has been reported to lower Total Antioxidant Capacity (TAC) levels (Kashyap et al., 2005; Sun et al., 2006).

In accordance with the finding of this study on the influence of diabetes and hypertension on MDA, decreased antioxidant activity and reduced levels of Reactive Oxygen Species (ROS) scavengers (vitamins E and C and glutathione) have been reported to contribute to oxidative stress (Taddei et al., 1998). Although studies have revealed no clear benefit of antioxidant supplementation no improvement in blood pressure (Heart Protection Collaborative Group 2002; Vivekananthan et al., 2003), the present study however indicated that hypertension and diabetes influence vitamin E and nitric oxide levels. Also, short-term oral high-doses of zinc, vitamin C, β-carotene and alpha-tocopherol have been reported by Galley et al. (1997) to lower blood pressure, possibly via increased availability of nitric oxide. Furthermore glucose; which is a component of diabetes, has been reported to alter the balance between free radicals and nitric oxide in endothelial cells by nitric oxide exerting its vasodilatory and antioxidant effect and this deleterious effect is said to occurs in endothelial cells exposed to glucose, which, in fact, favours the formation of oxygen and in turn promotes oxidation (Cosentino et al., 1997). Hence, the reduce nitric oxide which acts as a potent inhibitor of the lipid peroxidation chain reaction by scavenging propagatory lipid peroxyl radicals, reported in this study may not be unrelated to the presence of hypertension and diabetes.

The increase oxidative stress status and reduction in nitric oxide reported in this study by the hypertensive and diabetes conditions either existing alone or in combination may be the contributory factors to cardiovascular diseases. This fact is supported when one view the pathological role of oxidative stress in vascular diseases as previously stated by Madamanchi et al. (2005).

**CONCLUSION**

Conclusively, judging by the findings of this study, hypertension and diabetes, either existing alone or in
combination have a negative impact on oxidative stress and antioxidant status. By implication, the reported CVD reported among diabetics and hypertension may be related to the impact these conditions have on oxidative stress and antioxidant status.

REFERENCES


