Association of Cell Adhesion Molecules, Glycated Haemoglobin and Some Haematological Parameters with Diurnal Variation of Blood Pressure among Hypertensives

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Abstract

This study involves 50 hypertensive not on therapy, 50 hypertensives on therapy and 50 apparently healthy control between the ages of 18 and 70 years attending FMC Owerri. Fasting venous blood was collected for the determination of adhesion molecules such as serum P and E selectins, glycated haemogloblin and total white blood cells. The serum selectins were estimated using enzyme linked immunoabsorbent assay (ELIZA). While glycated haemogloblin and total white blood cells were estimated using standard methods. The Independent Student t test was used for statistical analysis. Results: The levels of P-Selectin(19.15±2.84) and E-Selectin (37.19±1.29) were significantly increased in hypertensives not on drugs (p<0.05),when compared with the control (7.09±0.87 and 12.55±2.46) respectively. Similarly, the levels of glycated haemogloblin (5.15±2.84) and total white blood cell count (8.79±0.40) were significantly increased in hypertensives not on drugs (P<0.05)when compared with the control (4.29±0.48 and 4.72±0.62) respectively. However, the levels of P and E-Selectins, glycated haemogloblin and Total white blood cell count were significantly decreased among hypertensives on therapy when compared with hypertensives not on therapy (p<0.05), The result suggests, that hypertensives are linked with increased P-Selectin and E-Selectin level which may be useful for predicting the severity of hypertensives

Keywords: *cell adhesion molecules, glycated haemoglobin, haematological parameters, blood pressure, hypertensives*

INTRODUCTION

Hypertension is another name for high blood pressure. It can lead to severe complications and increases the risk of heart disease, stroke, and death Blood pressure is the force exerted by the blood against the walls of the blood vessels. The pressure depends on the work being done by the heart and the resistance of the blood vessels[1].

Hypertension and heart disease are global health concerns. The World Health Organization (WHO) suggests that the growth of the processed food industry has impacted the amount of salt in diets worldwide, and that this plays a role in hypertension.

Lifestyle factors that increase the risk include excess salt in the diet, excess body weight, smoking, and alcohol use (Poulter *et al.,* 2015).Normal blood pressure is 120 over 80 mm of mercury (mmHg), but hypertension is higher than 130 over 80 mmHg [2]. Acute causes of high blood pressure include stress, but it can happen on its own, or it can result from an underlying condition, such as kidney disease. Unmanaged hypertension can lead to a heart attack, stroke, and other problems. Lifestyle factors are the best way to address high blood pressure.

Medical guidelines define hypertension as a blood pressure higher than 130 over 80 millimeters of mercury (mmHg), according to guidelines issued by

the American Heart Association (AHA) in November 2017. The cause of hypertension is often not known [3]

Around 1 in every 20 cases of hypertension is the effect of an underlying condition or medication. Chronic kidney disease (CKD) is a common cause of high blood pressure because the kidneys do not filter out fluid. This fluid excess leads to hypertension. A number of risk factors increase the chances of having hypertension [4].

Hypertension is more common in people aged over 60 years. With age, blood pressure can increase steadily as the arteries become stiffer and narrower due to plaque build-up Some ethnic groups are more prone to hypertension. Being overweight or obese is a key risk factor, Consuming large amounts of alcohol regularly can increase a person's blood pressure, as can smoking tobacco [5]. The lifetime risk is the same for males and females, but men are more prone to hypertension at a younger age. The prevalence tends to be higher in older women. Cardiovascular disease, diabetes, chronic kidney disease, and high cholesterol levels can lead to hypertension, especially as people get older. Other contributing factors include:, physical inactivity, a salt-rich diet associated with processed and fatty foods, low potassium in the diet, alcohol and tobacco use, certain diseases and medications . Hence, it is of great relevance to note the frequency of adhesion molecules, glycated haemoglobin and total white cell count and their relationship with hypertension.

Cell adhesion molecules (CAMs) are a subset of cell adhesion proteins located on the cell surface involved in binding with other cells or with the extracellular matrix (ECM) in the process called cell adhesion [6]. In essence, cell adhesion molecules help cells stick to each other and to their surroundings. Cell adhesion is a crucial component in maintaining tissue structure and function. In fully developed animals, these molecules play an integral role in creating force and movement and consequently ensure that organs are able to execute their functions. In addition to serving as "molecular glue", cell adhesion is important in affecting cellular mechanisms of growth, contact inhibition, and apoptosis. Oftentimes aberrant expression of CAMs will result in pathologies ranging from frostbite to cancer [7].

CAMs are typically single-pass transmembrane receptors and are composed of three conserved domains: an intracellular domain that interacts with the cytoskeleton, a transmembrane domain, and an extracellular domain[6]. These proteins can interact in several different ways. The first method is through homophilic binding, where CAMs bind with the same CAMs. They are also capable of heterophilic binding, meaning a CAM on one cell will bind with different CAMs on another cell. The final type of binding occurs between cells and substrate, where a mutual extracellular ligand that binds two different CAMS [8].

There are four major super families or groups of CAMs: the immunoglobulin super family of cell adhesion molecules (IgCAMs), Cadherins, Integrins, and the Super family of C-type of lectin known as selectin. One classification system involves the distinction between calcium-independent CAMs and calcium-dependent CAMs[9].

Endothelial dysfunction is a common feature in hypertension, and is associated with inflammation, increased levels of circulating soluble adhesion molecules, and atherosclerosis [10].

On the other hand, Glycated hemoglobin (HbA1c) is a form of hemoglobin that is covalently bound to glucose[11]. Hemoglobin, a protein within red blood cells that carries oxygen throughout the body. When hemoglobin is exposed to glucose in the blood, they are bound together through the glycation process. It is measured primarily to determine the three-month average blood sugar level and can be used as a diagnostic test for diabetes mellitus. Diabetes and hypertension often co-occur and share risk factors. Hypertension is known to predict diabetes. However, hyperglycemia also may be independently associated with future development of hypertension [12].

A white blood cell (WBC) count is a test that measures the number of white blood cells (WBCs) in the blood. WBCs, also called leukocytes, are an important part of the immune system. These cells help fight infections by attacking bacteria, viruses, and germs that invade the body white blood cells in the body [13].

Elevated white blood cell (WBC) count is considered to be prospectively associated with cardiovascular disease. However, its relationship to hypertension, independent of smoking and other established cardiovascular risk factors, is not clear, especially among women [14].

Hence, it is of great importance to determine the status of some adhesion molecules,total white blood cell count and glycated haemoglobin in hypertensive subjects

MATERIALS AND METHODS

Experimental Design

The subjects were grouped into 50 newly diagnosed hypertensives not on therapy, 50 hypertensives on therapy and 100 control. Hypertensive patients who gave their consent and are absent from every other disease were only involved. Subjects that have no evidence of hypertension and are apparently healthy served as control The morning, afternoon and evening blood pressure were recorded..

Sample Collection

Five (5) milliliters of blood sample was collected by standard venopuncture method[15] from each participant. Two (2) ml was dispensed into EDTA container for total white cell count and glycated haemogloblin while the remaining was dispensed into dry bottle for other analysis and was centrifuged to get the serum for the analysis

The Serum selectins were determined by enzyme linked immunoabsorbent assay (ELIZA) using standard commercial kits (Melsin China) While glycated haemogloblin was determined by Trivelli *et al.*,[16]. Also, Total white blood cell count was determined [17].

Statistical Analysis

The values were expressed as mean ± standard deviation. The significant difference between the mean value of control and experimental group was determined by one way analysis of variance (ANOVA) with post hoc t-test. $P<0.05$ was considered as statistically significant.

RESULTS

The results are presented as follows

Table 4.1. *Mean ± S.D of Diurnal Variation of E & P Selectin, TWBC and HbA1c among hypertensive on drugs*

Parameters Morning Evening P Value			
E Selectin	32.7±1.51	32.85±1.55	0.81
P Selectin	12.21±1.01	12.29±0.60	1.00
HbA1c	5.2±0.51	5.27±0.52	0.923
TWBC	6.80±0.56	8.90±0.55	0.45
Systolic Blood Pressure	141.32±16.74	144.04±15.27	0.399
Diastolic Blood Pressure	93.68±12.13	94.60±12.25	0.707

Table 4.1 Represent the Mean ± S.D of diurnal variation of E & P Selectin, TWBC and HbA1c among hypertensive on drugs

The Mean distribution of adhesion molecules of morning and evening were not significantly difference (P>0.05), the mean ± SD of morning E Selectin is 32.7±1.51 while the evening E Selectin is 32.85±1.55.

P Selectin values of morning and evening were not significantly difference (P>0.05) 12.21±1.01 and 12.29±0.60 respectively.

The mean ± S.D of HbA1c for morning and evening were not significant (p>0.05) 5.2±0.51and 5.27±0.52 respectively.

The mean ±S.D of TWBC were 6.80±0.56 and 8.90±0.55 for the morning and evening respectively and there was no significant difference (P>0.05).

The mean ± SD of the morning and evening systolic blood pressure were not significant (P>0.05) 14. 32 ± 16.74 and 144.04 ± 15.27 respectively.

The mean ± SD of the morning and evening diastolic blood pressure were not significant (P>0.05) 93.65 ± 12.13 and 94.60 ± 12.25 respectively.

Table 4.3. *Mean ± S.D of Diurnal Variation of E & P Selectin, TWBC and HbA1c among hypertensive not on drugs*

Parameters	Morning	Evening	P Value
E Selectin	36.69 ±1.22	37.36 ±1.30	0.42
P Selectin	18.75 ± 20.0	19.71 ±4.21	0.67
HbA1c	5.57 ± 4.4	5.64 ±0.43	0.81
TWBC	8.73 ±0.39	8.80 ±0.40	1.00
Systolic Blood Pressure	131.00 ±12.52	133.20 ± 11.84	0.526
Diastolic Blood Pressure	84.88 ± 8.9	86.68 ±5.7	0.324

Table 4.3 Shows the Mean ± S.D of Diurnal Variation of E & P Selectin, TWBC and HbA1c among hypertensive not on drugs.

The mean ± S.D of E Selectin shows that there was no significant difference (P>0.05) in diurnal variation of this parameter, 36.69 ± 1.22 and 37.36 ± 1.30 for the morning and evening respectively.

The mean ± S.D of P Selectin were 18.75 ± 20.0 and 19.71 ± 4.21 for the morning and evening respectively and also shows no significant difference (p>0.05)

The mean ±SD of HbA1c for the morning and evening were not significant (P>0.05) 5.57 ± 4.4 and 5.64 ±0.43 respectively and there was no significant difference (P>0.05)

The Mean± S.D of TWBC were 8.73 ±0.39 and 8.80 ±0.40 for the morning and evening respectively.

The mean ± of SD for the morning and evening systolic blood pressure shows no significant difference (P>0.05) 131.00 ± 12.52 and 133.20 ± 11.84 respectively.

The mean ± SD for the morning and evening diastolic blood pressure also shows no significant difference (P>0.05) 84.88 ± 8.9 and 86.68 ± 5.7 respectively.

Table 4.7. *Comparative analysis of hypertensive not on drugs against those on drugs*

Parameters	Not on drugs	On drugs	P Value
E Selectin	37.19 ± 1.29	32.79 ± 1.5	0.00
P Selectin	19.1 ± 2.84	12.28 ± 0.7	0.00
Hb1Ac	5.61 ± 0.42	5.2 ±0.52	0.00
TWBC	8.7 ± 0.4	6.8 ±0.55	0.00

The E-Selectin, P-Selectin, HbA1c and TWBC values were found to be significantly different (p<0.05) between hypertensives on drugs and those not on drugs.

DISCUSSION

Hypertension is a public health problem in which the blood pressure in the arteries is persistently elevated. High blood pressure typically does not cause symptoms .Hypertension remains an important public health challenge in Owerri Nigeria because it increases the risk for cardiovascular disease. Effective blood pressure management has been shown to decrease the incidence of stroke, heart attack and heart failure [18].

It was observed from the study that the levels of E-selectin and P-selectin, were significantly increased (P<0.05) in hypertensives that were not on therapy when compared with the control. Indeed, these increase in E and P selectin could be This linked to oxidative stress, because E-selectin and P-selectin were increased in plasma concentrations in hypertensives compared with control. Hence, there could be a possible relationship between this molecule and the endothelium-dependent response to acetylcholine in the forearm of essential hypertensive patients. The degree of vasodilation induced by acetylcholine is considered an index of endothelial dysfunction. This is in line with the work of [19] . Probably due to hemodynamic load caused by high BP, development of structural vascular changes that reduce the vessel capacity to dilate may occur. This shows a much more robust relationship of E-selectin plasma levels with indices of structural microvascular changes. The possibility might exist that the same stimuli able to increase E-selectin expression in vascular endothelium, such as the "inflammatory" cytokines interleukin-1 and tumor necrosis factor, are also able to cause or contribute to microvascular structural alterations, including smooth muscle cell remodeling and collagen synthesis. The increased E-selectin expression, by fostering leukocyte accumulation, might be a mechanism itself of structural vascular alterations in large arteries, because of the wide array of enzymatic products and secondary cytokines produced by emigrated leukocytes[20].

Also, the levels of glycated haemogloblin were significantly increased(P<0.05) in hypertensive that were not on therapy when compared with the controls. This is in line with the work of Julie *et al.,*[12] who also reported that the higher level of HbA1c was associated with an increased risked of hypertension in subjects not on drugs when compared with the non-hypertensive subjects. Individuals with elevated

HbA1c ,even without a prior diabetes diagnosis, are at increased risk of hypertension.HbA1c is a known predictor of incident heart disease and stroke. Our result suggest that the association of HbA1c with cardiovascular risk may be partially mediated by the development of hypertension.

It was observed that total white blood cells count were significantly increased in hypertensive not on therapy when compared with control (P<0.05). This is in agreement with the work of Anoop *et al.,*[21]. However its relationship to hypertension ,independent of the lifestyle and other established cardiovascular risk factors, is not clear. Although various risk factors have been implicated in the development of hypertension, some of which include genetic, environmental, psychosocial, and inflammatory factors. Links between inflammation and hypertension have associated with increased white blood cell count (WBC) [22]. Majority of the biological mechanism that has been suggested to explain the effect of elevated WBC on hypertension involves chronic low grade inflammation. Inflammation alters endothelial function, causing inability to produce nitric oxide and prostacycline, which results in the loss of vasodilator, antithrombotic, and anti-artherogenic properties of the vascular endothelium [23]. Also, stimulated leucocytes have an increased tendency to adhere to vascular endothelium, which may cause capillary leucocytosis, and subsequently increase vascular resistance. Elevated white blood cell (WBC) may also be a marker of a state characterized by increased catecholamine levels or sympathetic nervous activities, which can increase blood pressure and may eventually result in sustained hypertension[22].

WBC (leukocytes), which are the main fighter cells of the immune system and psychosocial stress have been implicated as risk factors in hypertension and there is substantial evidence for the plausibility of psychosocial influence on inflammation. There are also substantial evidences that stress and other psychosocial factors influence immunity. Stress and psychosocial factors may influence immunity through direct innervations of the central nervous system or through neuro-endocrine immune pathway. Based on knowledge of the kinetics and potential mechanisms of the way stress affects the immune response in the healthy individual, further research activities demonstrated that leukocytes from individuals with chronic inflammation differ in their response to acute psychosocial stress or adrenergic and corticoid stimulation in comparison to immune-competent cells from healthy subjects [24]. Studies have indicated that physical activity has positive impact on the human immune system and its functioning. Physical activity is consistently observed to be associated with reduced chronic inflammation and it has been reported that WBC is inversely related to the physical activity [25]. Also, data from numerous smaller studies suggest that regular physical activity has the potential to reduce circulating levels of several inflammatory biomarkers. However, studies have implicated genetics, race and individual variability in immunity and markers of inflammation in hypertension. It is also unclear whether the changes in white blood cells as a result of continuous exercise training will commensurate with changes in psychosocial stress in hypertension or vice versa. Based on the results of the present study, it could probably indicate that psychosocial stress, elevated WBC and hypertension are interrelated [23].

Similarly, it was observed from the study that the levels of E-selectin and p-selectin, were significantly decreased in hypertensive on therapy when compared with the hypertensive not on therapy. This is in agreement with the work done by Hironobu *et al.,*[26]. This could probably indicate that hypertensives on therapy are protected against vascular damage in people with hypertension, not only by lowering blood pressure, but also by inhibiting the expression of selectins. Therapeutic treatment reduced the content of P-selectin in the platelets from patients with Hypertension. Hence, decreased blood pressure may reduce the rate of progression of atherosclerosis by affecting the expression of E- and P-selectin in the endothelium, the platelets, or both. Drugs may be protective against vascular damage in people with hypertension, not only by lowering blood pressure, but also by inhibiting the expression of selectins [27].

This study equally indicated that diurnal variation of E and P Selectin, TWBC and HbA1c among hypertensive on drugs were not significantly increased when compared in morning, afternoon and evening (P>0.05). This probably implied that diurnal period were not affected. In the same vein, the diurnal variation of E and P Selectin, TWBC and HbA1c among hypertensive not on drugs were not significantly increased when compared in morning, afternoon and evening(P>0.05). However, the diurnal variation of E

and P Selectin,TWBC and HbA1c among hypertensive on drugs and those not on drugs were significantly decreased when compared in morning, afternoon and evening($P > 0.05$). This decrease could be associated with the drug effects on adhesion molecules which affected the vascular vessels. This is in line with the work of Daniel *et al.,* [28]

In conclusion, the results of this study have shown that P and E selectins status are significantly high in hypertensive patients which may be associated with high levels of free radicals and oxidative stress. This could probably imply that P and E selectins may be helpful as diagnostic parameters in the management of hypertension..Also Individuals with elevated HbA1c ,even without a prior diabetes diagnosis, are at increased risk of hypertension.HbA1c is a known predictor of incident heart disease and stroke. Elevated Twbc is associated with incident hypertension among male and female independent of social habit.

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