Research Article

Assessment Of Serum Interleukin-18 And Some Markers Of Hypertension


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ARTICLE INFO

ABSTRACT

Hypertension is an increasingly important medical and public health challenge worldwide. It is associated with cardiovascular disease, insulin resistance, obesity, carbohydrate tolerance, hyperuricacidemia and atherosclerosis among other factors. The study aimed at assessing the serum level of interleukin-18 and some markers of hypertension. A total of 80 samples were collected; 40 samples were collected from hypertensive subjects and 40 samples from apparently healthy subjects to serve as control. The height and weight of each subject was measured using height gauge and bathroom scales to calculate BMI. The interleukin-18 level was estimated using Enzyme linked immunosorbent assay technique. The results revealed that interleukin 18, systolic and diastolic blood pressures were significantly increased (P<0.001) in hypertensive subjects compared with control while Interleukin-18 also increased with increasing age. Interleukin-18 levels significantly (P<0.001) correlated with systolic and diastolic blood pressure in hypertensive subjects and control. The study concluded that interleukin 18 which is a pro-inflammatory cytokine is a contributing factor to the pathogenesis and progression of hypertension since interleukin 18 was significantly increased in hypertensive subjects and significantly correlated with blood pressure, BMI and increased age.
INTRODUCTION:
Hypertension is an increasingly important medical and public health challenge worldwide. It is associated with cardiovascular disease, insulin resistance, obesity, carbohydrate tolerance, hyperuricacidemia and atherosclerosis among other factors. The prevalence of hypertension in Nigeria has been shown to range from 8%-46.4% depending on the study target population, type of measurement and cut-off value used for defining hypertension. The prevalence was shown to be similar in men and women (7.9%-50.2% and 3.5%-68.8% respectively) and in the urban (8.1%-42.0%) and rural setting (13.5%-46.4%). However, a systematic review and Meta analysis estimated the overall prevalence of hypertension in Nigeria to be 28.9%. The causes of hypertension are multifactorial; although hypertension can be classified as either primary (essential) hypertension or secondary hypertension; about 90-95% of cases are categorized as 'primary hypertension' which means high blood pressure with no obvious underlying medical causes. It has been shown that 90-95% of all hypertension cases were categorized as essential hypertension, also known as primary hypertension or idiopathic hypertension. It is a heterogeneous disorder as different patients have different factors that cause high blood pressure. The cause of essential hypertension is still unknown but it is considered as the sum of interaction between genetic and multiple environmental factors.

Experimental studies have shown that interleukin-18 enhances atherosclerosis through release of interferon gamma and induces expression of inflammatory cytokine interleukin-6 (IL-6) in the vascular endothelial and smooth muscle cells.

Visceral fat is a relevant source of proinflammatory cytokines which are significantly elevated in serum of obese subjects. It has been proposed that the vascular systemic inflammation produced by adipose tissues contributes to the development of hypertension, since inflammation produces endothelial dysfunction.

It has been shown that Interleukin-18 provides powerful information on future fatal cardiovascular events across the entire spectrum of patients with stable coronary artery disease (CAD) and patients with unstable CAD. Therefore, the assessment of serum interleukin 18 in Nigeria’s population will be of immense value in the diagnosis of the aetiology of hypertension. Thus, the study aimed to assess serum interleukin-18 and some markers of hypertension and establish whether there is relationship between interleukin-18 and the markers.

MATERIALS AND METHODS
A total of eighty (80) subjects were investigated and classification was based on age and therapy. The subjects consist of 40 known hypertensive subjects and 40 apparently healthy subjects who served as control. Informed consent in written form was obtained from the subjects after due explanation before they participated in the study. Anthropometric measurement (body weight and height) was carried out in the subjects. Body weight was obtained using bathroom scales and height was obtained using a height gauge. Blood pressure was taken from the non dominant arm using appropriate cuff size and mercury sphygmomanometer. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were the first and the fifth koroktoff sounds respectively.

Venous blood sample of four millilitres (4ml) was collected from the cubital fossa and dispensed into a plain bottle (non anticoagulant bottle). The blood was allowed to clot and centrifuged at 12000rpm for 5 minutes to separate the serum from cells. The sample was stored at a temperature of -20 degree Celsius for up to 21 days before assayed. The method of analysis of interleukin 18 is based on Enzyme linked immunosorbent assay (ELISA).

The results obtained were subjected to statistical analysis using SPSS 17. All
parameters were expressed as mean±SD. Student ‘t’ was the tool of choice and values were found to be statistically significant or otherwise at P<0.001 (version 21.0 software, SPSS Inc. Chicago, Illinois, USA).

RESULTS
Interleukin-18, Systolic blood pressure and diastolic blood pressure were statistically increased (P<0.001) when the levels in hypertensive subjects were compared with that of control. Body mass index was not statistically significant at (P<0.001) when the level in hypertensive subjects was compared with that of control. When all parameters were analysed at different age group, ages 40-49 years predominates with an increased BMI followed by below 40years, 50-59years and 60years and above. Interleukin-18 levels significantly (P<0.001) correlated with systolic and diastolic blood pressure in hypertensives and controls. Interleukin-18 levels did not significantly correlate with ages in hypertensives and controls.

Table 1: Interleukin-18 and other markers in hypertensive subjects and control subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>Hypertensives (N=40)</th>
<th>Control (N=40)</th>
<th>T values</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interleukin-18 (Pg/ml)</td>
<td>688.3±1143.45</td>
<td>81.8±121.8</td>
<td>3.446</td>
<td>0.001***</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>154.8±10.03</td>
<td>115.0±6.04</td>
<td>21.390</td>
<td>0.000***</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>97.7±5.63</td>
<td>74.1±2.76</td>
<td>13.459</td>
<td>0.000***</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>24.9±3.86</td>
<td>24.0±3.69</td>
<td>1.047</td>
<td>0.2976</td>
</tr>
</tbody>
</table>

***--Significant at p<0.001

Table 2: Correlation of interleukin-18 and other markers in hypertensive subjects and controls.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Systolic BP</th>
<th>Diastolic BP</th>
<th>Age</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensive subjects (n=40)</td>
<td>0.717**(0.000)</td>
<td>0.833**(0.000)</td>
<td>0.047 (.775)</td>
<td>-0.119 (0.464)</td>
</tr>
<tr>
<td>Controls (n=40)</td>
<td>0.765**(0.000)</td>
<td>0.679**(0.000)</td>
<td>-0.171 (.293)</td>
<td>0.019 (0.958)</td>
</tr>
</tbody>
</table>

**. Correlation is significant at the 0.001 level
*. Correlation is significant at the 0.05 level
DISCUSSION

Interleukin-18 is a proinflammatory cytokine which may play an important role in heart failure via their effects on myocyte contractility, inflammation, cell death and endothelial function. In this study, there was a significant (P<0.001) increase in the level of interleukin-18 compared with control, making it evident that hypertension is associated with increased interleukin-18 levels. This finding agrees with other findings\textsuperscript{13,14} which show that it is clear that circulating levels of IL-1\(\beta\) and IL-18 are increased in hypertension\textsuperscript{13,14}. Interleukin-18 significantly correlates with blood pressure in hypertensive subjects and control. When all parameters were analysed at different age group, ages 60 years and above predominates with an increased interleukin 18 level followed by 50-59 years, then ages 40-49years and below 40 years. This finding shows that interleukin-18 is a biomarker of ageing because interleukin-18 levels increases with age in hypertension. It also shows a positive correlation between interleukin-18 and ages in hypertensives. The increase in body weight and BMI with advanced age has been reported\textsuperscript{15,16}. Body mass index (BMI) was also assessed and compared between the two groups in this study. There was no statistically significant difference (P<0.001) between BMI in hypertensives subjects compared with control. These findings agree with other studies which support a strong relationship between BMI, blood pressure across and age in developed and developing countries\textsuperscript{17}. This has also been supported by other works which showed that body composition variables such as weight, skin fold thickness are significantly correlated with blood pressure in adults\textsuperscript{18,19}.

Furthermore, in this study, there was a statistically significant increase (P<0.001) between systolic BP in hypertensive subjects compared with control subjects. This finding indicate that systolic blood pressure is a classical parameter in the diagnosis of hypertension; it also gives an indication that the use of hypertensive drugs has blood pressure lowering effects\textsuperscript{20}. This finding also agreed with other researches which show that patients with elevation of both systolic blood pressure and diastolic blood pressure have been shown to benefit from drug treatment\textsuperscript{21,22}. When all parameters were analysed at different age groups; age 50-59years predominates with a higher systolic and diastolic blood pressure followed by 60years and above, 40-49years and below 40years. The increase in blood pressure with age is mostly associated with structural changes in the arteries and especially with large artery stiffness\textsuperscript{23}. An elevation in systolic blood pressure
pressure is the most prevalent type of hypertension in those aged 50 and above, occurring either de novo or as a development after a long period of systolic-diastolic hypertension with or without treatment.

CONCLUSION
Thus, since interleukin 18 was significantly increased in hypertensive subjects and was significantly correlated with blood pressure, BMI and increased age, the study concluded that interleukin 18 which is a pro-inflammatory cytokine is a contributing factor to the pathogenesis and progression of hypertension. This may also be or contribute to the reason for the recent increase in sudden death in humans.

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REFERENCES


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