Estimation the Level of Superoxide Dismutase 1 among Iraqi Patients with Hypertension

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Abstract

Background: Hypertension plays a critical role as a risk factor for cardiovascular mortality, encompassing conditions like coronary artery disease, organ damage, congestive heart failure, and cerebrovascular diseases. Furthermore, hypertension can lead to increased oxidation and peroxidation reactions due to elevated blood pressure and blood flow. Objective: This study aimed to evaluate the levels of superoxide dismutase in the sera of patients diagnosed with hypertension. Materials and Methods: The study involved 60 hypertensive patients who exhibited no significant abnormalities, such as liver disease, cardiomyopathy, renal disease, diabetes mellitus, congestive heart failure, or thyroid disease. Additionally, 25 healthy individuals, matched by age and sex to the patient group, were included in the study. The age range of the participants was between 32 and 70 years. The level of superoxide dismutase 1 in the sera was measured using an enzyme-linked immunosorbent assay (ELISA). Results: The results demonstrated a significant increase in the activity level of superoxide dismutase in hypertensive patients (732.91 ± 82.68 pg/ml) compared to the control group (590.63 ± 47.69 pg/ml). Conclusion: These findings have the potential to contribute to the diagnosis and management of hypertension, offering insights into the role of superoxide dismutase activity in the disease process.

Keywords: High blood pressure, SOD1, ELISA and Systolic blood pressure.
**Introduction**

High blood pressure (HBP), or hypertension, is defined by a persistent rise in the force of blood against artery walls. Kidney failure, heart disease, and stroke are just a few of the health problems that may arise as a result of this condition. Hypertension is characterized by a systolic blood pressure level equal or more than 140 mmHg while a diastolic blood pressure level equal or more than 90 mmHg, this can be triggered by a range of factors, including lifestyle choices, genetics, and underlying medical conditions (1, 2). The diagnosis of hypertension usually involves measuring two types of blood pressure: systolic pressure, which is the pressure during heart contraction, and diastolic pressure, which is the pressure when the heart is resting between beats. A normal blood pressure reading is 120/80 mmHg, whereas a reading of 140/90 mmHg or higher is considered hypertension (3, 4). Hypertension is a significant risk factor for various serious health problems, including kidney failure, heart disease, and stroke (5). The typical approach to treatment includes lifestyle adjustments like changes in diet and exercise, as well as medication when required. It is crucial for people with hypertension to keep track of their blood pressure regularly and collaborate with their healthcare provider to manage the condition effectively (6, 7).

Reactive oxygen species (ROS) are highly reactive molecules that contain oxygen and are formed as natural byproducts of normal cellular metabolism (8). While a certain level of ROS is necessary for normal cellular processes, excessive ROS can cause damage to cells and tissues, leading to oxidative stress. Excessive ROS can be caused by a variety of factors, including environmental pollutants, radiation, certain medications, and poor diet (9). Additionally, ROS can be produced as a result of chronic inflammation or in response to infections. The body has natural defense mechanisms to neutralize ROS, such as antioxidants, which can scavenge and neutralize ROS before they cause damage (10). Therefore, maintaining a balance between ROS production and neutralization is essential for healthy cellular function. SOD is found in almost all living organisms, including humans, and it is particularly abundant in cells that are exposed to high levels of oxygen, such as those in the lungs and liver (11). The enzyme is composed of different subunits, each of which requires a specific metal cofactor for its activity. The three main types of SOD are copper-zinc SOD (Cu-Zn SOD), manganese SOD (Mn SOD), and extracellular SOD (EC-SOD), which differs in their location within the cell and their cofactor requirements. Cu-Zn SOD is located in the cytosol and mitochondria, and it requires both copper and zinc for its activity. Mn SOD is located in the mitochondria and requires manganese for its activity. EC-SOD is found in the extracellular space and requires copper, zinc, and heparin for its activity (12, 13). Given the essential role of SODs in disease, this study aimed to measure a plasma concentration of SOD1 in patients with HBP.

**Materials and Methods**

**Sample Collection**

During the period of October to December 2022, blood was collected from 60 patients who were diagnosed with hypertension at Medical City Hospital, along with 25 healthy individuals. A volume of 3 ml of blood was extracted intravenously and collected into a vacuum gel tube. Once the blood clotted, the serum samples were separated through centrifugation for about 15 minutes (at approximately 1000 x g). The resulting serum was then transferred into small Eppendorf tubes and stored in a freezer at -20°C until further analysis.

**Determination of Superoxide dismutase**

SOD1 levels were measured using an ELISA kit from Elabscience in the USA. This kit works on the principle of Competitive-ELISA, where the micro ELISA plate has pre-coated SOD1 and the test was done according to provided sheet of instructions. The optical density (OD) is measured at a wavelength of 450 nm using an Automatic ELISA reader (PKL PPC 230 ITALIA paramedical). Finally, by comparing the OD of the samples to the standard curve, it can be performed to determine the concentration of SOD1 in the tested samples.

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Statistical analysis

SPSS-The Statistical Package for the Social Science (version 25.0) was utilized for statistical analysis. An independent sample t-test was employed to make comparisons between groups, and a statistically significant difference was identified as P<0.05.

Results

For this study, 60 patients who had recently been diagnosed with hypertension were selected consecutively. The mean systolic and diastolic blood pressures (mmHg) of the hypertensive patients were identified to be significantly elevated than those of the control group (P<0.001), as depicted in Table (1) and Figure (1).

![Figure (1): Systolic and diastolic blood pressure in HBP patient and control](image1)

In case of SOD1 level, the mean concentrations of plasma SOD1 in control group is 590.63 ± 47.69 pg/mL, while the medians were found to be significantly higher among hypertensive patients 732.91 ± 82.68 pg/mL ), as depicted in Table (1) and Figure (2).

![Figure (2): SOD1 level in HBP patient and control](image2)
Table (1): The levels of systolic/diastolic blood pressure and SOD1 in both hypertensive patients and control subjects

<table>
<thead>
<tr>
<th>Number</th>
<th>HBP</th>
<th>Control</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>145.66 ± 10.09</td>
<td>128.26 ± 8.92</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>90.62 ± 9.88</td>
<td>79.56 ± 6.66</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Superoxide dismutase (pg/mL)</td>
<td>732.91 ± 82.68</td>
<td>590.63 ± 47.69</td>
<td>&lt;0.0001***</td>
</tr>
</tbody>
</table>

Discussion

Research finding suggests that a hypertensive patient, who is characterized by high blood pressure, is associated with an increase in both systolic and diastolic blood pressures. This is an important consideration in the diagnosis and management of hypertension. The increase of blood pressure is often a result of the narrowing and hardening of the blood vessels, which can be caused by elements such as cholesterol elevation, obesity, absence of physical activity, and stress. As the blood vessels become narrower and less flexible, it becomes more difficult for blood to flow through them, leading to an increase in blood pressure (14, 15). This increase can affect both the systolic and diastolic pressures, as systolic pressure measures the pressure in the arteries when the heart contracts, while diastolic pressure measures the pressure when the heart is resting between beats (16). Over time, the elevated blood pressure can cause damage to the blood vessels and organs, increasing the risk of cardiovascular disease and other health problems. Therefore, it is important to monitor and manage high blood pressure through lifestyle changes, medication, and other interventions to reduce the risk of these complications (17).

Hypertension is a prevalent disease that significantly increases the risk of morbidity and mortality related to cardiovascular disease, particularly coronary artery disease. It can also cause various alterations in lipoproteins and oxidation-peroxidation processes, where Ox-LDL is a significant risk factor. SOD activity is the first line of defense against oxidative stress, and it is closely linked to these processes (18). Based on the study's findings, the patient group had lower serum levels of SOD activity compared to the control group.

Patients with hypertension and heart disease may have higher levels of oxidative stress than healthy individuals, which may explain the higher percentages of SOD1 seen in these individuals. According to previous study hypertension and cardiovascular disease may both be influenced by oxidative stress (19). It should be noted that excessive amounts of SOD1, despite its antioxidant properties, can result in increased oxidative stress. Studies involving transgenic animals have demonstrated that elevated levels of SOD1 can lead to heightened sensitivity to oxidative stress (20). This could be driven on by a rise in hydrogen peroxide, a byproduct of the dismutation process. Three potential mechanisms driven by SOD1 have been identified by Kowald et al. These include the exchange between the oxidized and reduced forms of SOD during the detoxification of superoxide radicals, the reaction of hydrogen peroxide with CuZnSOD that produces hydroxyl radicals, and the action of superoxide radicals as chain breakers (21, 22). Studies conducted both experimentally and clinically have suggested that oxidative stress precedes the onset of elevated blood pressure and may be an initiating factor for the progression from prehypertension to hypertension (23, 24). Finally, study concludes that patients with HBP exhibited increased levels of SOD1 in their plasma. These enzyme levels could potentially serve as useful biomarkers in the future for diagnosing or managing HBP.
References


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تقدير مستوى SOD1 في امتصال المرضى العراقيين الذين يعانون من ارتفاع ضغط الدم

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الخلاصة

الخلاصة العلمية: يلعب ارتفاع ضغط الدم دورًا مهمًا وعامل خطير في الوفيات نتيجة امراض القلب الوعائية من ضمنها مرض الشريان التاجي، وتفاعل الأعضاء، ونقص القلب الاحتفالي، والأمراض الدماغية الوعائية. علاوةً على ذلك، يمكن أن يؤدي ارتفاع ضغط الدم إلى زيادة تفاعلات الأكسدة والبيروفكسيد بسبب الزائدة في سرعة تدفق الدم. هدف هذه الدراسة إلى تقييم مستوى SOD1 في مصل المرضى المصابة بارتفاع ضغط الدم. المواد وطريقة العمل: تضمنت الدراسة 60 مريضًا يعانون من ارتفاع ضغط الدم فقط وبأجل مرضى أخرى مثل أمراض الكبد، أو ارتفاع ضغط الدم، أو أمراض القلب، أو أمراض الكبد، أو صور القلب الاحتفالي، أو أمراض القلب الوعائي. بالإضافة إلى ذلك، تم تجميع 25 فردًا سليمًا كمجموعة التحكم. تراوحت أعمار المشاركين بين 32 و70 سنة. بعدها تم قياس مستوى SOD1 في مصل المرضى الذين يعانون من ارتفاع ضغط الدم. النتائج: أظهرت النتائج زيادة في ارتفاع ضغط الدم في مصل الطرف الاليزة الراصد (92.91 ± 82.46 محارم / مل) مقارنة بلفة السطحية (63.90 ± 47.69 محارم / مل). الاستنتاج: يبين هذه النتائج أهمية قياس مستوى SOD1 لفهم الإدمان كمؤشر على التشخيص أو السيطرة على ارتفاع ضغط الدم، وكنذلك يمكن أن يعتبر أحد الأسباب أو العوامل المهمة في نشوء المرض أو تطوره.

الكلمات المفتاحية: ارتفاع ضغط الدم، SOD1، الآلزيا، ضغط الدم الوعائي.