Original Article

The Level of Nitric Oxide Synthase and Nitric Oxide in Hypertensive Women

Ghassan Salah Ahmed[1], Falah Hassan Shari[2], Hala A. Alwan[3], Rasha Fadhel Obaid[4], Haider Abdulkareem Almashhadani[5], Mustafa M. Kadhim[6]

[1]Department of Clinical Pharmacy, College of Pharmacy University of Basrah, Iraq

[2]Department of Clinical Laboratory Sciences College of Pharmacy University of Basrah, Iraq

[3]College of Dentistry, Al- Farahidi University, Baghdad, Iraq.

[4]Department of Biomedical Engineering, Al-Mustaqbal University College, Babylon, Iraq.

[5]Dentistry Department, Al-Rasheed University College, Iraq

[6]Medical Laboratory Techniques Department, Al-Turath University College, Iraq

Email: Ghassan.ahmed@uobasrah.edu.iq

Abstract

Hypertension is a cardiovascular problem with high rates of epidemiology and risks of morbidity and mortality in the global area. Nitric oxide (NO) is one of the reactive oxygen species (ROS) that produced from L-arginine by nitric oxide synthase (NOS) enzyme. NO involves in various vital processes in human health, one of which is the modulation of vasoconstriction and relaxation of the vascular system. We have aimed to investigate the link between NO and NOS with hypertension in women. The relationship between NO and NOS, as well as the usefulness of them as indicators of hypertension risks were subjects of study in this article. The results have revealed that hypertensive women had significant ($P<0.05$) lower levels of NO (15.07±3.41 IU/mL) and NOS (9.79±2.08 ng/mL) in their serum compared to normotensive healthy women. The results have shown strong relationship between nitric oxide synthase/nitric oxide and hypertension in women. The reduction of NOS in the serum of hypertensive women leads to a reduction in the circulation levels of NO. Nevertheless, the NOS reduction may not be the only reason for the reduction of NO, which can be caused by elevated oxidative stress. Based on these results, we suggest the controlling of NOS and NO in hypertensive people to reduce the risks of cardiovascular problems.

Keywords: Hypertension, NO, NOS, oxidative stress.

1. INTRODUCTION

Essential hypertension is a long-term increase in the blood pressure caused by a variety of genetic as well as environmental factors. Its prevalence increases with age, regardless of the method of measurements or the diagnostic thresholds used. Essential hypertension affects 25–35 percent of the adult population in both developed and developing countries, as well as up to 60–70 percent of individuals in their seventh decade. Because of a shared underlying etiology, hypertension clusters with other cardiovascular risk factors as abdominal obesity, dyslipidemia, glucose intolerance, hyperinsulinemia, as well as hyperuricaemia [1].

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Address for correspondence: Ghassan Salah Ahmed, Department of Clinical Pharmacy, College of Pharmacy University of Basrah, Iraq
Email: Ghassan.ahmed@uobasrah.edu.iq

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Although measuring blood pressure is a simple procedure for identifying a cardiovascular disease risk phenotype, treating raised blood pressure alone is insufficient to reduce the associated cardiovascular disease risk to its optimal level, as well as formal cardiovascular disease risk estimation is recommended [2]. During the previous four decades, global mean blood pressure has remained steady or declined somewhat. From the other hand, hypertension is growing increasingly common, particularly in low as well as middle income nations (LMICs). According to estimates, 31.1 percent of the world's population (1.39 billion) had hypertension in 2010. Adult hypertension is more prevalent in low and middle income nations (31.5 percent of the population, or 1.04 billion people) than in high income ones (28.5 percent, 349 million people). low potassium intake, obesity, High salt intake, alcohol consumption, physical inactivity, as well as a poor diet could explain a few of the geographical variability in hypertension prevalence [3].

Reactive oxygen species (ROS) is termed to every oxygen containing material with high reactivity [4] and linked to beneficial and harmful effects in the human biological system [5-8]. ROS includes superoxide radical (O2.-), nitric oxide (NO.), hydroxyl radical (HO.), and several other materials have been identified [4, 9]. The redox signaling takes ROS as mediators to perform the beneficial functions in the biological system [10], while the harmful effects involved in the oxidative damage of proteins (enzymes, structural proteins, transporter proteins, receptors, etc.), lipids of the membranes, and nucleotide sequences [11, 12]. NO is an important regulator in the vasoconstriction and relaxation of the vascular system, as well as platelet disaggregation [13], and also it acts to transmit the messages of the central nervous system in a way resembles that of neurotransmitters [14]. NO is produced from the guanidine nitrogen of L-arginine via the catalytic activity of nitric oxide synthase (NOS) enzyme [15]. We have designed this study to determine NO and NOS in the serum of hypertensive women, to predict their role in elevated blood pressure. The relationship between NO and NOS, as well as the usefulness of them as indicators of hypertension risks were subjects of study in this article.

2. Materials and Methods

2.1. Patients

The women hypertensive patients were documented in the consultancy of Emergency Department at Al-Yarmook Teaching Hospital (Baghdad, Iraq). The volunteered people were informed about the standard criteria of the research and agreed to become a volunteers in this work. 60 hypertensive women patients were selected for the study from December 2021 to February 2022, and controlled with 30 healthy volunteered women at matched ages.

2.2. Methods

The hypertensive women patients and healthy women control were donated a vein blood upon 8 hours of fasting. Then the blood was centrifuged in a medical centrifuge (4000 rpm for 10 minutes), and the plasma was stored in a deep freezer at -20 °C to be analyzed for NO and NOS by using a sandwich ELISA kits (MyBioSource, USA), and the measurement was performed on ELISA microplate reader (Human, Germany).

2.3. Statistics

The data were processed statistically on the computer by a program from IBM called SPSS version 26.0, for mean comparisons in an independent sample t-test, and the relationship between NO and NOS were calculated according to the Pearson correlation. At last, the sensitivity of protein carbonyl as diagnostic marker for hypertension in women was determined by the receiver operating characteristic (ROC) curve through measuring area under the curve (AUC) of each variable.

3. Results

The characteristics of the volunteered women are contained in Table 1. Age was shown non-significant (P>0.05) differences between the hypertensive women patients (43.97±10.33 year) and control normotensive women (41.67±10.59 year). Also, the body mass index (BMI) was non-significantly (P>0.05) different between hypertensive women patients (24.96±2.10 kg/m2) and control women (24.71±2.09 kg/m2). Furthermore, from the diagnostic criteria of hypertension in women, systolic (155.67±6.99 mmHg) and diastolic (95.87±8.36 mmHg) BP were significantly elevated in hypertensive women.

Table 1: Volunteered women characteristics.

Parameter	Hypertensive Women	Control Women	*P*-value
N	60	30	-
Age (year)	41.67±10.59	43.97±10.33	0.331
BMI ($kg.m^{-2}$)	24.71±2.09	24.96±2.10	0.605
Diastolic BP (mmHg)	74.27±4.68	95.87±8.36	0.0001
Systolic BP (mmHg)	113.37±4.31	155.67±6.99	0.0001
NO (IU/mL)	35.34±4.74	15.07±3.41	0.0001
NOS (ng/mL)	13.38±2.71	9.79±2.08	0.0001

The level of NO was observed to be significantly (P<0.05) lower in serum of hypertensive women patients (15.07±3.41 IU/mL) compared to the serum of control women (35.34±4.74 IU/mL). Furthermore, hypertensive women have

shown significant (P<0.05) lower levels of NOS enzyme (9.79±2.08 ng/mL) in their serum compared to the serum of control normotensive women (13.38±2.71 ng/mL).

The results have shown significant positive correlation between the determined NO level and NOS levels in the serum of hypertensive women patients, as shown in Table 2. Also, a significant negative correlation was obtained in hypertensive women between NO and systolic BP, and between NOS and diastolic BP.

Table 2: Correlation in hypertensive women patients.

Parameter	NO		NOS	
	r	*p*-value	r	*p*-value
NOS (ng/mL)	0.970	0.0001	-	-
Age (year)	0.002	0.985	0.030	0.820
BMI (kg.m^{-2})	-0.116	0.378	-0.100	0.449
Systolic BP (mmHg)	-0.178	0.175	-0.173	0.187
Diastolic BP (mmHg)	-0.853	0.0001	-0.853	0.0001

The ROC curve of NO has indicated the usefulness of this biomarker in the diagnosis of hypertension disease in women. NO has shown excellent sensitivity (AUC = 1.0, P<0.0001) in the diagnosis of hypertensive women patients comparing to the healthy controls, as shown in Figure 1.

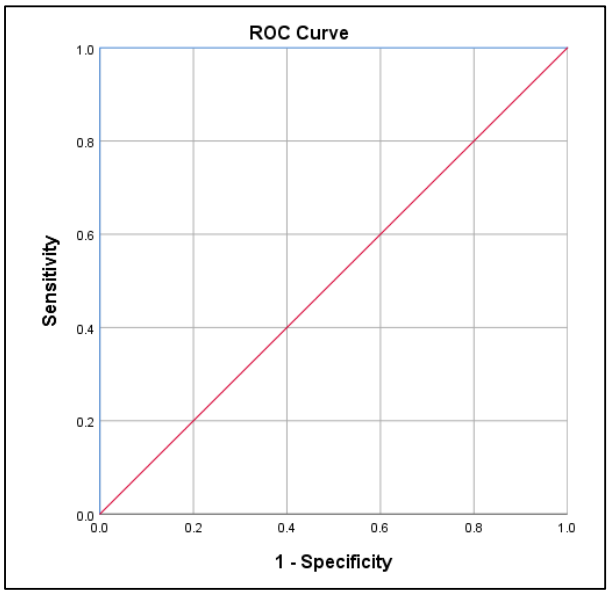

Figure 1: The ROC curve of NO in the diagnosis of hypertension disease in women.

The ROC curve of NOS has indicated the usefulness of this biomarker in the diagnosis of hypertension disease in women. NOS has shown good sensitivity (AUC = 0.847, P<0.0001) in the diagnosis of hypertensive women patients comparing to the healthy controls, as shown in Figure 2.

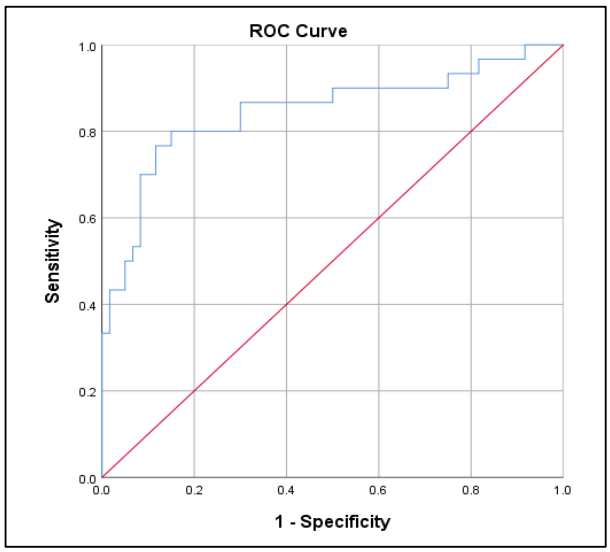

Figure 2: The ROC curve of NOS in the diagnosis of hypertension disease in women.

4. Discussion

The results have shown that both nitric oxide as well as nitric oxide synthase enzyme are linked to the blood pressure in hypertensive women. There levels were reduced significantly in the serum of hypertensive women. Barbadoro et al. have reported that hypertensive patients had significant low levels of NO compared to normotensive people. The authors have concluded that there is an association between oral microbes, NO, and hypertension [16]. Zhang et al. have indicated a reduction in the levels of NO in hypertensive people, and linked this reduction to the elevated ROS and oxidative stress [17].

Nayak et al. have reported a significant reduction in the levels of serum nitric oxide in patient with essential hypertension. The workers have concluded that serum NO can be an important causative factor in the progress of essential hypertension [18,19]. In the study of Kalaivani et al. the workers have indicated a reduction of endothelium NOS enzyme in hypertensive rats [20]. Nevertheless, Hammed et al. have showed significant elevated levels of inducible nitric oxide synthase in serum of hypertensive people with chronic kidney diseases [21].

Despite NO is considered as a species of ROS, it can react with another species of ROS (O2.-) and yield peroxynitrate (ONOO-), which was reported as a pathway of NO reduction in hypertension by Galleano et al. [22]. In this regard, ROS levels were reported to be significantly elevated in serum of hypertensive obese women by Taay and Mohammed [4]. Hence, NO can be affected in hypertension by the reduction of its producing enzyme (NOS), and by the elevated levels of ROS.

5. Conclusions

The results have shown strong relationship between nitric oxide synthase/nitric oxide and hypertension in women. The reduction of NOS in the serum of hypertensive women leads to a reduction in the circulation levels of NO. Nevertheless, the NOS reduction may not be the only reason for the reduction of NO, which can be caused by elevated oxidative stress. Based on these results, we suggest the controlling of NOS and NO in hypertensive people to reduce the risks of cardiovascular problems.

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