World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-14, September 2022
ISSN: 2749-3644

THE CHANGES OF NITRIC OXIDE SERUM LEVELS IN PATIENTS WITH END-STAGE RENAL DISEASE

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Article history:

Received: July 17th 2022
Accepted: August 17th 2022
Published: September 30th 2022

Abstract:

Chronic Renal Failure (CRF) is a term used to describe an irreversible decline in renal function that often occurs over a number of years. In many situations, an initial insult to the kidney function leads to additional nephron loss and the requirement for dialysis or kidney transplantation End stage renal disease (ESRD) is the term used to describe this ailment. Patients with chronic kidney disease (CKD) are at an increased risk of cardiovascular (CVD) morbidity and mortality, mainly due to atherosclerosis. Decreased production or reduced bioavailability of nitric oxide (NO) can result in endothelial dysfunction (ED). Multiple mechanisms are known to cause a state of NO deficiency in patients with CKD. this study compares the levels of (NO), and its ratios, in ESRD patients and healthy controls.

Keywords: Chronic Renal Failure, nitric oxide, urea, phosphorus.

METHODS: In all, 70 ESRD patients 30 males and 40 females with ages ranging from (30 to 55) years old and 30 controls 13 males and 17 females with ages ranging from (25 to 60) years old were included in the study. All participants' biochemical characteristics, demographic information, and serum nitric oxide concentrations were examined.

RESULTS: According to our research, people with chronic renal failure had highly significant progressive decrease in serum levels of nitric oxide than did healthy controls. Nitric oxide had positive correlation with urea and phosphorus.

CONCLUSION: We found differences in nitric oxide levels that might be used to detect chronic renal failure

AIMS: Analyze of serum levels of nitric oxide (NO) in end-stage renal disease (ESRD) and Healthy individuals.

INTRODUCTION: CRF, or chronic renal failure, is the most common public health issue affecting the aged population globally. Having a damaged kidney is the main cause of CRF. According to the glomerular filtration rate (GFR), there are five stages of CRF, and stage 5 (GFR 15 ml/min/1.73m2) is sometimes referred to as an end-stage renal disease (ESRD)[1]. Due to impaired renal function, there is a buildup of toxins and extra water in CRF. The preferred method for treating ESRD and removing built-up toxins from the body is dialysis. Patients receiving dialysis have a cardiovascular risk that is 10–20 times greater than that of healthy individuals. Dialysis and inflammatory kidneys both impact endothelial function, increasing the risk of hypertension and heart issues. Therefore, the risks associated with receiving dialysis should be understood by both doctors and patients. Patients with CRF need to be informed as soon as possible about the disease, treatments, dietary requirements, and other factors necessary for managing the condition and leading a normal life[2]. Numerous endothelium activities are altered by oxidative stress, including vasomotor tone modulation and kidney function effects. Nitric oxide (NO•) appears to be inhibited by superoxide and other reactive oxygen species (ROS) in conditions like hypertension, diabetes, hypercholesterolemia, and smoking. You might lose NO because to these traditional risk factors, which also help to explain why they're preparing for arterial hardening [3]. ROS are raise in hypertension in response to vessel stimulation by mechanical stretch or AngII. reaction of ROS with endothelium released NO inhibits vasodilatory or antisclerotic effects of NO and thus can aggravate the disease [4] . (Ang II) levels are raised but ROS is actually dicline , probably due to the accompanying increase in super oxide dismutase (SOD) expression [5].This capacity to boost antioxidant defenses might be sufficient to shield blood vessels from mild oxidative stress, enabling ROS to serve as signaling molecules. However, compensatory mechanisms are insufficient and have pathological consequences when ROS output is excessive [6]. Nitric oxide (NO), a gas formed from the metabolism of L-arginine by constitutive endothelial NO synthase, is the best described of the anti-

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atherogenic chemicals that endothelial cells may create and emit [7].

An endogenous modulator with a variety of biological activities is nitric oxide (NO). Hypertension and vasculopathy have been linked to chronic suppression of NO synthases (NOS). Numerous research have investigated the impact of CRF on NO metabolism in light of these factors with the hypothesis that NO deficit may be implicated in the pathophysiology of cardiovascular and other consequences of uremia. This review aims to provide a concise summary of the impact of CRF on the following factors: (1) the bioavailability of the NO substrate, L-arginine; (2) the expression of NOS isoforms in the relevant organs; (3) the interaction of NO with reactive oxygen species, which are known to be increased in CRF; and (4) the accumulation of uremic inhibitors of NOS.[8].

Nitric oxide production by the vascular endothelium keeps a vasodilator tone that is vital for controlling blood flow and pressure levels. Nitric oxide facilitates cell-cell signaling in the brain. Nitric oxide is also produced by several neurons that were previously categorized as non-adrenergic and non-cholinergic in the peripheral nervous system. This straightforward gaseous molecule therefore serves a multitude of physiological purposes. suitable for therapeutic manipulations: Nitric oxide donors can be given (for hypertension, atherosclerosis, gastrointestinal, and genitourinary problems) or nitric oxide gas can be inhaled to counteract impaired nitric oxide synthesis (in chronic pulmonary hypertension or adult respiratory distress syndrome). Creating techniques to counteract nitric oxide's harmful and cytotoxic effects is the largest problem.[9].

MATERIALS AND METHODS

Study participants: The current study was conducted in AL-Yarmouk teaching hospital, during the period from October 2021 to March 2022. The present study included 70 (30 males and 40 females) ESRD patients from 30 to 60 years old and 30 (13 males and 17 females) healthy control group ranging from 25-60 years old. This study was approved by the Department of Chemistry, College of Science, Al-Nahrain University.

Sample collection: Patients and healthy individuals provided seven milliliters of venous blood placed into gel tubes for 15 minutes to coagulate. Serum was isolated from blood samples by centrifugation at 1840 x g for 15 minutes at room temperature. The serum was separated into aliquots and kept at -70°C until testing.

Measurement of Body Mass Index: BMI was measured by dividing weight (in Kilograms, Kg) by height squared (in meter, m) for each participant.

Biochemical analysis: serum levels of nitric oxide were measured using enzyme-linked immune-sorbent assay (ELISA) provided by (SunLong ,china). The photometric method was used to evaluate the serum urea provided by (Linear, Spain) and phosphorus provided by (Spinreact, China).

Statistical Analysis of Parameters: Demographic and biochemical data in the present study were performed using GraphPad Prism software version 8.0.2 (San Diego, California, USA). T-test unpaired was performed to assess mean ± standard deviation (STD) and significant differences (P-value) among means of the two studied groups. Correlations between parameters in the present study were estimated with Pearson's correlation coefficient. $P \leq 0.05$ was considered statistically significant.

RESULTS

The table below summarizes the demographic characteristics of the two groups investigated (End-stage renal disease (ESRD and Control). The preliminary analysis revealed that There were no significant differences in age or BMI between the ESRD and control groups (p=0.5565).

The difference in nitric oxide concentrations between the two groups is seen in Table below .were substantially lower (p <0.0001) in the ESRD group than in the control group, according to statistical analysis. as shown in figure below.

Pearson's correlation coefficient was calculated between nitric oxide was related positively to serum urea (r = 0.3568, P= 0.0383), and correlated significantly with phosphorus (r = 0.4647, P = 0.0174).

Parameter	Control	Patients	P-Value	Significant
Age(year)	53.39±8.2	54.53±6.9	0.5565	NS
BMI	29.6 ± 2.4	30.2 ± 3.4	0.0993	NS
Nitric Oxide	15.97±3.258	4.809±1.075	<0.0001	HS
Urea	27.21 ±4.100	136.3 ± 37.39	<0.0001	HS
Phosphorus	3.200 ± 0.6325	5.507 ± 1.703	<0.0001	HS

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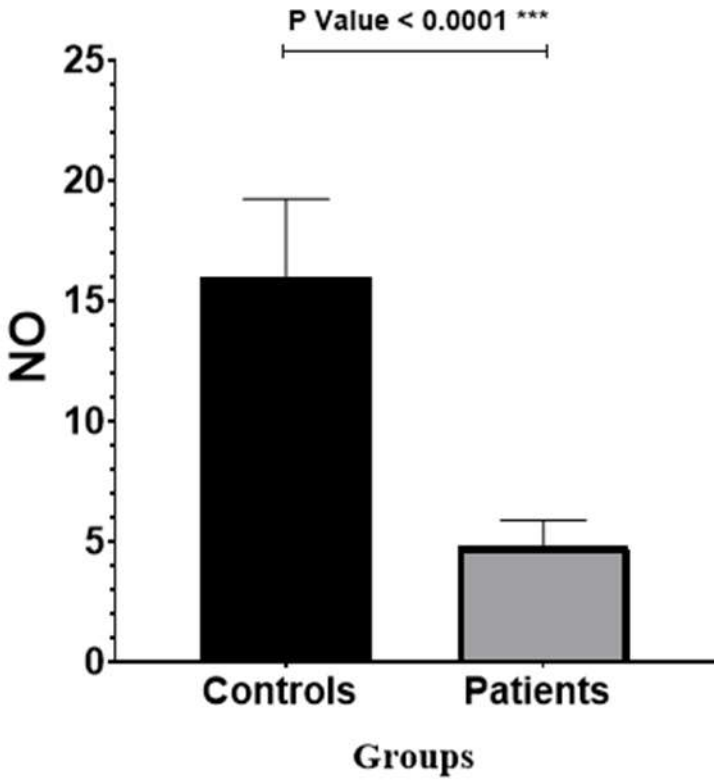

The figure shows Nitric oxide Levels in Patients and Control Group

DISCUSSION

End-stage renal disease (ESRD) has been linked in several studies to oxidative stress.In our research, we looked at the serum levels of nitric oxide in patients with ESRD to see what role oxidative stress have in the disease's etiology. To evaluate the oxidative state in CKD patients, there was a highly significant progressive decrease in the mean value of NO in patients when compared with the controls ($P < 0.001$).In the study of Mochammad Thaha[10] showed that there was a highly significantly decreased in Nitric oxide level in dialysis patients with CRF($p<0.05$), NO is one of the important components of blood vessels, which regulate the main health reporting paths [11] . Through the creation of reactive oxygen and nitric species, NO production is impaired in a disease state. Reduced NO production is recognized as a precursor to endothelial dysfunction. [12]. Reactive Nitrogen Species (RNS), which are frequently present in kidney disease, and excessive ROS are two characteristics of oxidative stress. ROS, which include superoxide anion (O2), hydrogen peroxide (H2O2), and hydroxyl radical, are byproducts of aerobic metabolism (OH-). Peroxynitrate (ONOO-) is created when the superoxide anion (O2-) reacts with NO [13], It causes NO consumption and lipid peroxidation. Oxidative stress causes a deficit of NO, which causes endothelial dysfunction because it causes the inactivation of oxygen free radicals and the conversion of NOS into superoxide producers. Reduced NO production results in less vasodilation that is endothelium-dependent. A condition of low NO can be caused by a few methods. [14]. Numerous research that have looked at the connection between NO and CKD have found that the illness may often be distinguished by systemic, endothelial, and renal NO insufficiency regardless of the fundamental cause of the condition. According to some studies, this NO shortfall considerably adds to the progressive character of CKD, and endothelial NO insufficiency undoubtedly plays a role in the cardiovascular damage seen in patients with renal failure. Reversing eNOS suppression and/or increasing the damaged kidney's capacity to generate NO are potential ways to retain remaining renal function and/or slow the rate of progression to end stage. [15]. Numerous different vascular processes are tightly regulated by the endothelium-derived NO. The accelerated atherosclerosis and increased cardiovascular mortality seen in CKD patients had been suggested to be caused by a lack of vascular NO. Multiple mechanisms exist for how NO deficit manifests in CKD. End-stage uremic factors in plasma prevent l-arginine from entering cells, which may result in a "net"

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substrate deficit. Inhibitors of endogenous NO synthetase, particularly asymmetric dimethylarginine, also increase (ADMA) [16] .

CONCLUSION

Our findings reveal that nitric oxide levels are significant progressive decrease. Therefore, these alterations may play a key role in the development of end-stage renal disease (ESRD).

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