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Maternity and Reproductive Health Sciences

OPEN ACCESS RESEARCH ARTICLE

Pattern of Nitric Oxide Levels and Endothelial Nitric Oxide Synthase in Preeclamptic Women Visiting General Hospital Owerri

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Received date: **June 11 ,2024:** **Accepted date:** **July 04, 2024:** **Published date:** **July 08, 2024**

Citation: Nwokeji Calistus Muodebe[1*] (2024), Pattern of Nitric Oxide Levels and Endothelial Nitric Oxide Synthase in Preeclamptic Women Visiting General Hospital Owerri**, Maternity and Reproductive Health Sciences (MRHS) 1(1), DOI: 10.1875/mrhs.2024/005.**

Abstract:

A condition unique to pregnancy, preeclampsia results in morbidity and mortality in both the mother and the fetus. Preeclampsia's precise etiology is unclear. However, the pathophysiology of preeclampsia is greatly influenced by endothelial dysfunction. The purpose of this study was to quantify the levels of maternal serum NO and endothelial nitric oxide synthase (eNOS) in preeclamptic women. In this study, 100 preeclamptic women and 100 normotensive women served as the control group. The conventional approach was used to assess the levels of nitric oxide and nitric oxide synthase. When comparing the levels of Nitric Oxide Synthase and Nitric Oxide in preeclampsia (4.10 ± 1.96 ng/mL and 6.11 ± 3.41 µmoles/L) to those in healthy pregnant women (7.22 ± 3.01 ng/mL and 12.52 ± 3.30 µmoles/L, respectively), at $p<0.05$, the differences were statistically significant. The study reveals that altered endothelial function in preeclampsia was indicated by lower endothelial Nitric Oxide Synthase and nitric oxide.

Key Words: Endothelial Dysfunction, Healthy Pregnant Women, Preeclampsia

Introduction

Preeclampsia (PE) is a human pregnancy condition that is often detected after 20 weeks of gestation and is associated with 3-8% of pregnancies with potentially life-threatening complications. It also leads to maternal and fetal morbidity and death[1]. The high rate of maternal fatalities in developed nations and the higher range in underdeveloped nations are explained by this complication [2].

This multiorgan illness affects the kidney, liver, brain, and endothelium.The placenta, which serves as the fetus and mother's interface, is crucial in the start of preeclampsia. The precise mechanism underlying the disease remains unclear despite a great deal of research. However, one of the contributing factors to the pathogenesis of preeclampsia, which includes oxidative stress, platelet and thrombin activation, inflammation, and an imbalance between angiogenic and anti-angiogenic molecules, is poor and shallow placentation with impairment of spiral artery remodeling with endothelial dysfunction[3].

The endothelium is a crucial metabolizing and endocrine organ that also plays a significant role in the regulation of immunology, inflammation, and angiogenesis. It also plays a vital role in the control of blood fluidity, platelet aggregation, and vascular tone [4,5].

Sufficient uteroplacental blood is needed throughout pregnancy, and this depends on vasodilation. Thus, the endothelium's ability to produce vasodilator molecules is crucial for preserving a healthy pregnancy by controlling blood pressure. The symptoms of preeclampsia, including hypertension, edema, and proteinuria, have been associated to impaired endothelial function [6, 7]. The enzyme nitric oxide synthase (NOS) is in charge of producing nitric oxide, or NO. NADPH, NOS, and tetrahydrobiopterin work together to transform l-arginine into l-citrulline and NO. Nitric oxide is a gaseous and extremely hazardous substance. NO aids in the destruction of foreign invaders and cancer cells by the mammalian immune system because of its toxicity, short half-life (1–5 s), and diffusibility. Because it stimulates the manufacture of cGMP, it also functions as a cellular signal. NOSs are the same subunit dimers. NOS is a source of heme, tetrahydrobiopterin, flavin mononucleotide (FMN), and flavin adenine dinucleotide (FAD). To promote electronic interaction between the heme and the tetrahydrobiopterin-binding site, the site is located in close proximity to the heme [8]. At the interface where the subunits join, residues from both subunits create the tetrahydrobiopterin-binding site; the pterin ring is positioned between a tryptophan residue from one subunit and a phenylalanine from the other.

The tetrahydrobiopterin of NOS loses only one electron, producing a biopterin radical, as opposed to the two electrons lost in AAHs. Another distinction between NOS and the AAHs is that biopterin is still linked to NOS both before and after catalysis [9].Increased creation of free radicals is necessary for some physiological functions in various forms of preeclampsia, but too many of them can lead to oxidative stress and cell damage. The changes linked to free radicals are mostly mediated by enzymes. Nitric oxide synthase (NOS), which catalyzes the synthesis of nitric oxide (NO), is one of them. Three distinct variants of this enzyme—NOS1, NOS2, and NOS3—are produced by distinct genes.Intercellular signaling, immune system support, and blood vessel function regulation are possible roles for them [10,11]

In this study, the level of Endothelial Nitric Oxide Synthase and Nitric Oxide Levels in women with preeclampsia were evaluated to provide information on their status in Owerri Imo State, Nigeria.

Methods

Research design

This case control study was carried out from March 2018 to May 2019 at General Hospital Owerri.

Research subjects

100 pregnant women between the ages of 20 and 32 who had been clinically diagnosed with preeclampsia in the third trimester (30–40 weeks) and were receiving care at General Hospital Owerri served as the study's subjects. The preeclampsia diagnostic criteria of elevated blood pressure (both systolic and diastolic), proteinuria, and pathological edema were used to select the subjects. One hundred healthy, normotensive pregnant women in their third trimester (30–40 weeks) who were also between the ages of 20 and 32 were used as normal controls. The study excluded patients with a prior history of hypertension, diabetes, or renal illness.

Blood collection

In all subjects 4 ml of fasting venous blood was collected into plain bottles. The serum was separated by centrifuging the whole blood in Westerfuge (model 684) centrifuge at 5,000g for 10 minutes and was used for serum Endothelial Nitric Oxide Synthase and Nitric Oxide

Biochemical assay

The enzyme-linked immunosorbent assay (ELISA) method was used to determine the amount of endothelial nitric oxide synthase in serum.
Using Griess reagent, which forms a chromophore that can be measured at 543 nm in a spectrophotometer when NO reacts with 3% sulphanilamine and 10% ethylenediamine dihydrochloride, one can determine the serum nitric oxide content.

Statistical analysis

The values were expressed as mean ± standard deviation. The independent Student t-test was used to calculate the significant differences at $p<0.05$.

Ethical clearance

Consent as well as ethical approval was obtained from the ethical committee of the Hospital

Result

Table 1. Endothelial Nitric Oxide Synthase and Nitric Oxide level in preeclampsia subjects and controls

Parameters	control	preeclampsia	p
Nitric Oxide Synthase (ng/mL)	4.10 ± 1.96	7.22 ± 3.01*	0.001
Nitric Oxide (µmoles/L)	6.11 ± 3.41	12.52 ± 3.30*	0.0000

The levels of Nitric Oxide Synthase and Nitric oxide in preeclampsia (4.10 ± 1.96 ng/mL) and (6.11 ± 3.41 µmoles/L) were significantly decreased when compared with heathy pregnant women (7.22 ± 3.01 ng/mL) and (12.52 ± 3.30 µmoles/L) respectively at $P<0.05$

Discussion

There is a connection between preeclampsia and higher antioxidant usage. Toxins and volatile free radicals, also known as atoms or groups of atoms with an unpaired electron, are neutralized by antioxidants. Relatively speaking, these include reactive oxygen species (ROS) that generate free radicals and set off a chain reaction in biological systems [12].

When compared to a normal pregnancy, the endothelium Nitric Oxide Synthase and Nitric Oxide were significantly lower in preeclampsia in this study. This is in line with a study that discovered that, in comparison to normal pregnancy, plasma from pre-eclamptic women also had a significant drop in mitochondrial endothelial nitric oxide synthase and nitric oxide.Nitric oxide concentrations and serum endothelial nitric oxide synthase levels in healthy pregnant women and preeclampsia

. Comparing preeclampsia to healthy pregnant women, the results showed lower amounts of endothelial Nitric Oxide Synthase and Nitric Oxide levels. These results were in line with those of previous research [13, 14]. Endothelial Nitric Oxide Synthase has been shown to contribute to increased uterine arterial blood flow and utero-placental vascular changes in both the mother and the fetus, while preeclampsia is caused by reduced placental abnormalities, specifically in relation to the Nitric Oxide Synthase and Nitric Oxide pathway [15]. In fact, it has been observed that pre-eclamptic syncytiotrophoblasts express less nitric oxide and placental nitric oxide synthase. This particular feature discovery supports the biological role of nitric oxide synthase in the placenta. [16].

The current study and other investigations have connected vascular endothelial dysfunction to lower nitric oxide levels in preeclampsia, which may be caused by decreased nitric oxide synthesis or increased breakdown.The pathophysiology of preeclampsia, which results in inadequate placentation, damage to endothelial cells, and altered endothelial function, has been linked to numerous etiological causes [17]. Increased systemic vascular resistance and decreased placental perfusion brought on by a dysfunctional endothelium also worsen placental ischemia-reperfusion injury, promote lipid peroxidation, increased production of reactive oxygen species (ROS), and lower antioxidant status [18].

. Furthermore, mitochondria may be a source of reactive oxygen species (ROS) that contribute to the pathophysiology of preeclampsia by inducing cell death, endothelial dysfunction, and redox signaling [19].

conclusion

In comparison to a normal pregnancy, this study demonstrated a considerable decrease in endothelial nitric oxide synthase and nitric oxide levels in preeclampsia. This highlights the significance of tracking the amounts of Nitric Oxide and Nitric Oxide Synthase in the serum during prenatal exams in order to lower the risk of pre-eclampsia. Estimating these parameters in the maternal circulation may serve as markers of vascular impairment in preeclampsia since eNOS and nitric oxide may likely reflect endothelial dysfunction.

Conflict of interest

There is no conflict of interest.

References

1. Nnodim JK, Ihim A, Uduji HI (2012) Alterations in antioxidants enzymes and malondialdehyde status in preeclampsia. Asian Pacific J Trop Biomed S673 –8.

2. Maynard SE, Karumanchi SA (2013). Angiogenic factors and preeclampsia. Semin Nephrol 31:33-46.

3. Hansson SR, Nääv Å, Erlandsson L(2015). Oxidative stress in preeclampsia and the role of free fetal hemoglobin. Front Physiol 5:516

4. Laskowska M, Laskowska K, Terbosh M, Oleszczuk J(2013).. A comparison of maternal serum levels of endothelial nitric oxide synthase, asymmetric dimethylarginine and homocysteine in normal and preeclamptic pregnancies. Med Sci Monit 2013; 19:430-437.

5. Darkwa EO, Djagbletey R, Sottie D, Owoo C, Vanderpuye N, Essuman R, (2018). Serum nitric oxide levels in healthy pregnant women: a case-control study in a tertiary facility in Ghana. Matern Health Neonotol Perinatol 4(3):1-

6. Tabassum H, Al-Jameil N, Ali MN, Khan FA, Al-Rashed M(2015).. Status of serum electrolytes in preeclamptic pregnant women of Riyadh, Saudi Arabia. Biomed Res;26:219-24

7. Akhtar S, Begum S, Ferdousi S(2011).. Calcium and zinc deficiency in pre-eclamptic women. J Bangldesh Soc Physiol 6:94-9.

8. Igwe CU, Okafor PA, Ibegbulem CO, Okwara JE (2015). Effect of pre-eclampsia on plasma and erythrocytic divalent cation concentrations and their bioenergetics of transport. Asian J Med Sci 6:6:18-23.

9. Zawiejska A, Wender-Ozegowska E, Iciek R, Brazert J (2014).. Concentrations of endothelial nitric oxide synthase, angiotensin-converting enzyme, vascular endothelial growth factor and placental growth factor in maternal blood and maternal metabolic status in pregnancy complicated by hypertensive disorders. *J Hum Hypertens*; 28(11):670-676.

10. Dacaj R, Izetbegovic S, Stojkanovic G, Dreshaj S(2016)... Elevated liver enzymes in cases of preeclampsia and intrauterine growth restriction. *Med Arch* 70(1): 44-47.

11. Choi JW, Im MW, Pai SH(2002)... Nitric oxide production increases during normal pregnancy and decreases in preeclampsia. Ann Clin Lab Sci 32(3):257-263.

12. Yuquan Wu, Xu Xiong, William D. Fraser, Zhong- Cheng Luo. (2012).. Association of Uric Acid with progression to preeclampsia and development of adverse conditions in gestational hypertensive pregnancies. Am J Hypertens 25 (6): 711-717.

13. Magna M, Sitikantha N(2013)... Elevated levels of serum uric acid, creatinine or urea in preeclamptic women. Int J Med Sci Public Health; 2(1): 43-47.

14. Rutherford RA, McCarthy A, Sullivan MH, Elder MG, Polak JM, Wharton J.(1995) Nitric oxide synthase in human placenta and umbilical cord from normal, intrauterine growth-retarded and pre-eclamptic pregnancies. Br J Pharmacol 116(8):3099-3109.

15. Richard AD, Rutherford, Andrew McCarthy, Mark HF, Sullivan, Murdoch G Elder, (1995). Nitric oxide synthase in human placenta and umbilical cord from normal, intrauterine-growth retarded and preeclamptic pregnancies. Br J Pharmacol 116:3099-3109.

16. Kulandavelu S, whiteley KJ, Qu D, Mu J (2012), Bainbridge SA, Adamson SL. Endothelial nitric oxide synthase deficiency reduces uterine blood flow, spiral artery elongation and placental oxygenation in pregnant mice. Hypertension 60(1):231-238.

17. Rukmini M S, Kowsalya R, Pai B, Das P, Perriera J, Nandini M, *(2009)* Plasma adenosine deaminase activity and antioxidant status in preeclampsia compared to healthy pregnant and nonpregnant women. *Biomed Res* 20 (1): 15-20.

18. Jayabalan A (2013). Epidemiology of preeclampsia: impact of obesity. *Nutr Rev*2013; 71:S18-S25.

19. Daskalakis G (2015), Papapanagiotou A. Serum markers for the prediction of preeclampsia. *J Neurol Nephrol* 2015; 6(1):1-9.