ORIGINAL ARTICLE

Correlation between serum nesfatin-1 level and severity of preeclampsia — A case control study

Henan Dh Skheel Aljebory,[1] Zinah Muayad Abdalkareem,[2] Adnan Mohammed Jasim[3]

Abstract

Objectives: To investigate if serum levels of nesfatin-1 are correlated with the severity and presence of preeclampsia.

Method: The case-control study was conducted at the Department of Obstetrics, Al-Yarmouk Hospital, Baghdad, Iraq, from February to December 2018, and comprised pregnant women recently diagnosed with preeclampsia at 37-40 weeks of gestation. They were divided into equal groups of non-severe preeclampsia group A and severe preeclampsia group B, and normotensive pregnant women of comparable gestational age control group C. Serum nesfatin-1 level was measured using enzyme-linked immunosorbent assay, and its relation to preeclampsia and its severity was analysed. Data was analysed using SPSS 25.

Results: Of the 150 pregnant women, 50(33%) with mean age 27.8±6.4 years and gestational age 38.3±0.9 weeks were in group A, 50(33%) with mean age 28.5±6.5 years and gestational age 38.4±1.0 weeks were in group B, and 50(33%) with mean age 29.2±7.2 years and gestational age 38.4±1.0 weeks were in group C ($p>0.05$) Mean nesfatin-1 concentration was lower in group A and B compared to group C ($p<0.001$), and it was significantly lower in group B than in group A ($p<0.001$).

Conclusion: Decrease in serum nesfatin-1 level was found to be correlated with the development of preeclampsia and its severity.

Keywords: Preeclampsia, Nesfatine-1, Inflammatory factors. (JPMA 71: S-49 [Suppl. 8]; 2021)

Introduction

Preeclampsia (PE) is a multisystem disorder unique to pregnancy. PE pathology is unknown till now. Many theories regarding the aetiology have been proposed, but the focus of the studies has been varied. The PE pathophysiology is not fully understood. Its development process has two stages: maternal inflammatory response and abnormality of placentation.[1]

Pregnancy is usually associated with a systemic inflammatory response. The response is exaggerated in PE and can be responsible for the clinical manifestations of some of the physiologic alterations of normal pregnancy, like the immediate-phase reaction caused by an inflammatory reaction. Placenta is the important cause of the pathology. There are many other factors that might cause the inflammatory responses and they are still being investigated. The susceptibility of women with obesity, chronic hypertension (HTN), or diabetes mellitus (DM) to PE might be explained by chronic systemic inflammatory responses that these women have.[2]

Nesfatin-1 (NESF) is a nucleobindin-2 (NUCB2) hormone involved in various metabolic conditions and regulation of appetite, mainly expressed in different parts of the hypothalamus and present in the general circulation. NESF is also produced by pancreatic cells of both humans and rats. Its main function is reduction of the appetite. It usually leads to appetite loss and a feeling of satiety.[3] The B-cell of pancreas along with the NESF/NUCB2 in rats and mice, raises the possibility of NESF involvement in insulin production from the beta cells of pancreas.[4] Its levels in fasting were lower in patients with type 2 DM (T2DM), but its role is unknown in patients newly diagnosed with gestational DM (GDM).[5]

The current study was planned to measure serum NESF concentrations and to find if the NESF level has any relation with PE and its severity.

Patients and Methods

The case-control study was conducted at the Department of Obstetrics, Al-Yarmouk Hospital, Baghdad, Iraq, from February to December 2018. After approval from the Arab Board for Medical Specialisations (Scientific Council of Obstetrics and Gynaecology), the sample size was calculated using G-power calculator.[6]

The sample comprised of pregnant women with single

[1]College of Medicine, Al Mustansiriyah University, [2,3]AL Yarmouk Teaching Hospital, Baghdad, Iraq.

Correspondence: Henan Dh Skheel Aljebory. Email: hanandhali@yahoo.com

viable foetus recently diagnosed with preeclampsia at 37-40 weeks of gestation. Those excluded were pregnant women with multiple gestations, gestational HTN, nephrotic syndrome, metabolic disorder, chronic HTN, Diabetes Mellitus or epilepsy. Also excluded were smokers and those having a congenitally abnormal baby.

After taking verbal consent from the participants, they were divided into equal groups of non-severe PE group A, severe PE group B, and normotensive pregnant women of comparable gestational age control group C.

Demographic and clinical data was collected, including age, height, weight, gestational age, past obstetric and medical history. General and obstetric examinations were carried out for each participant. The body mass index (BMI) was usually measured on the basis of pre-pregnancy weight. Non-severe PE was diagnosed on the basis of HTN, with two readings of systolic blood pressure (SBP) ≥140 mmHg and <160 mmHg, and/or diastolic blood pressure (DBP) ≥90mmHg and <110mmHg separated by a period of 4 hours, and proteinuria ≥0.3g/24h or ≥1+ on dipstick in the absence of urinary tract infection after 20 weeks of gestation in a previously normotensive woman.[7] Severe PE meant sustained elevation of SBP ≥160mmHg or DBP ≥110mmHg, or other signs of end-organ damage and significant proteinuria. SBP and DBP were usually recorded twice 4 hours apart with the patient in the sitting position. For the diagnosis of proteinuria, a urine dipstick test was used.[7] Further, 8ml blood were collected from the subjects during antenatal examination or on admission for delivery for serological analysis and other investigations. Blood samples were collected in vacutainer tubes without any anticoagulant, and were then separated by centrifugation and stored at -20°C till assessment. An enzyme-linked immunosorbent assay (ELISA) (Phoenix Pharmaceuticals, Inc., Burlingame, CA) was used to measure serum NESF levels.

Data was analysed using SPSS 25. Type of delivery was expressed as frequencies and percentages, and chi-square test was used for assessing the statistical association with PE. Continuous data was expressed as mean and standard deviation. Two-tailed analysis of variance (ANOVA) was used to compare the continuous parametric variables among the study groups.

Linear regression analysis was used to assess the amount of change in NESF caused by changes in the associated parameters.

Receiver operator characteristic (ROC) curve was used to study the parameters of NESF serums levels for the detection of PE and then its severity. P<0.05 was considered significant.

Results

Of the 150 pregnant women, 50(33%) with mean age 27.8±6.4 years and gestational age 38.3±0.9 weeks were in group A, 50(33%) with mean age 28.5±6.5 years and gestational age 38.4±1.0 weeks were in group B, and 50(33%) with mean age 29.2±7.2 years and gestational age 38.4±1.0 weeks were in group C (p>0.05). While there was no significant difference among the groups regarding BMI and type of delivery, the difference was significant with respect to the birth-weight of the neonate (Table-1).

There was significant association NESF with SBP, DBP and birth-weight, triglyceride (TG), and high-density lipoprotein (HDL) (-=0.001), but not with low-density lipoprotein (LDL) and total cholesterol (Table-2). Mean NESF concentration was lower in group A and B compared to group C (p<0.001), and it was significantly lower in group B than in group A (p<0.001).

ROC curve for serum NESF as a PE diagnostic marker suggested NESF <0.97ng/ml as the cutoff value.

ROC curve analysis was constructed for serum NESF as a diagnostic marker for PE severity. The cut-off value was 0.68ng/ml was predictive of PE severity with 94%

Table-1: Comparison of demographic features and gestational age at delivery, type of delivery and foetal birth-weight in the study groups.

Variables	Control (n=50) Mean ±SD	Pre-eclampsia		P-value
		Non-Sever (n=50) Mean ±SD	Sever (n=50) Mean ±SD	
Age (years)	27.8 ± 6.4	28.5 ± 6.5	29.2 ± 7.2	0.545
Body mass index (Kg/m^2)	28.6 ± 3.5	28.1 ± 2.8	29.3 ± 2.8	0.145
Gestational age (weeks); Mean ± SD	38.3 ± 0.9	38.5 ± 1	38.4 ± 1	0.675
Birth weight (Kg); Mean ± SD	3.1 ± 0.4	3.2 ± 0.5	2.7 ± 0.5	<0.001**
Type of delivery; No. (%)				
Normal vaginal delivery	30 (60%)	28 (56%)	20 (40%)	0.106
Caesarean section	20 (40%)	22 (44%)	30 (60%)	

**<0.01 Significant by ANOVA test; SD: Standard deviation.

Table-2: Correlation between nesfatin-1 and other parameters.

Variables	Nesfatin-1 (ng/ml)			Regression	
	Correlation coefficient (r)	Coefficient of determinant (r2)	P-value	Regression coefficients (B)	P-value
Age (years)	-0.001	0.00	0.986		
Body mass index (Kg/m^2)	-0.01	0.00	0.9		
Systolic Blood Pressure (mmHg)	-0.657	0.43	<0.001*	0.003	0.379
Diastolic Blood Pressure (mmHg)	-0.714	0.51	<0.001*	-0.02	<0.001**
Gestational age (weeks)	0.032	0.00	0.694		
Birth weight (Kg)	0.237	0.06	0.004*	-0.003	0.962
Triglycerides (mg/dl)	-0.16	0.03	0.05*	0.09	0.155
Cholesterol (mg/dl)	0.03	0.00	0.71		
HDL (mg/dl)	0.145	0.02	0.08		
LDL (mg/dl)	0.006	0.00	0.94		

*<0.05 significant by Pearson's bivariate correlation.
**<0.01 significant by linear regression analysis; regression formula [Y= 2.234 + (-0.02 X DBP).
HDL: High-density lipoprotein, LDL: Low-density lipoprotein.

sensitivity, 70% specificity and 84% accuracy.

Discussion

The current study found reduced NESF level in pregnant women diagnosed with PE. Lack of comprehensive understanding of PE pathophysiology is still impeding attempts to develop a specific medication or preventive approach.[8] It is well known that PE can adversely affect intrauterine growth rate (IUGR).[9] The weight of newborns was less in PE patients compared to the controls (p< 0.001).

The current study showed that serum NESF levels were associated with the development of PE and its complications. Studies have shown that obesity is a great risk factor for PE.[10,11]

NESF has a great role in the feeding behaviour regulation, like food intake and appetite regulation. Abaci et al.[12] showed the NESF levels were lower in overweight-obese children compared to control subjects, indicating that NESF can act as a link between PE and obesity. Anwar et al. showed significantly higher NESF level in obese when correlated with the group of controls.[13] The current study showed that serum NESF level correlated negatively with BMI. Tsuchiya et al. showed serum NESF was correlated negatively with BMI.[14] Zhao Y et al. showed NESF level correlated significantly with SBP and DBP.[15] Tang et al. stated that when NESF was given after head trauma, it caused reduction of nuclear factor kapa-B and reduced the concentrations levels of tumour necrosis factor-alpha, interleukin-6 (IL-6) and IL-1b in the brain tissues in rats.[16] Bonnet et al. wrote that NESF nerve cells in the hypothalamus increased during inflammatory stimulus of lipopolysacharides.[17] Vitoratos experienced that the anti-inflammatory role of NESF, and inflammation played a role in PE pathology.[18] Reyes et al. said that factors of metabolic syndrome were correlated with PE risk compared to the control pregnant women in Colombia.[19] Osaki et al. reported that peripheral or intravenous injection of NESF increased the blood pressure of mice and rats.[20]

Hamedani et al. stated that there was no correlation between serum NESF level and blood pressure in obese and normal-weight groups, which is in contrast to the current findings.[21] O Kovalyova et al. showed increasing NESF levels in patients suffering from essential HTN.[22] Cuijuan Zhang et al. experienced no differences between PE and non-PE groups with relation to age, BMI and lipid profile, but other parameters revealed differences between the groups regarding SBP, DBP, body-weight of the baby and serum NESF, which is line with our findings.[23] A Ghanbari-Niaki et al. found increased concentration of HDL induced by exercise and NESF affected by physical exercise.[24] Shaikh MK et al. showed decreased serum HDL level in hypertensive pregnant women compared to normotensive pregnant women, which is in line with our study.[25] Islam NA et al. said PE was associated with a significant elevation in triglyceride and fall in HDL concentration, which is also similar with the current findings.[26] Enquobahrie et al. found significantly higher levels of triglycerides in PE,[27] and this agrees with the current study.

The current study has several limitations, including a small sample size and having been done at a single centre.

Conclusions

There was a significant association between serum NESF level and PE as well as with PE severity.

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