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Assessment of serum afamin in patients with preeclampsia at third trimester

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Preeclampsia (PE) is a multisystem disorder associated with pregnancy. It is accompanied by a ten percent global neonatal and perinatal mortality rate. Human afamin (AFM) is a glycoprotein which bind vitamin E. It is primarily developed by hepatocytes in the liver and then secreted into the blood. Elevated serum afamin levels have been reported in hypertensive pregnancy complications such as Pregnancy Induced Hypertension (PIH). To evaluate afamin levels in preeclamptic women at third trimester and explore if there is any relation between Afamin and severity of preeclampsia, a case control study was performed in Chemistry and Biochemistry Department, College of Medicine, Al-Nahrain University, Baghdad, Iraq from July 2019 to March 2020. Forty-one patients and 30 participants in control group (normal pregnant women) joined this study. The preeclamptic and normal pregnancies were taken with cluster random sampling method. Afamin (AFM) levels were measured by enzyme-linked immune sorbent assay (ELISA). Serum afamin (AFM) was significantly ($p < 0.05$) elevated in pregnant women with preeclampsia 2.34 ±0.23 (ng/mL) compared with that in normal pregnant women group 1.63± 0.19 (ng/mL). Although serum AFM concentration significantly increased in Preeclamptic women, there was no significant association differences between mild and sever groups.

KEYWORDS

Afamin; preeclampsia; the severity of preeclampsia; third trimester of pregnancy.

Introduction

Preeclampsia is a multisystem disorder that occurs during pregnancy and cause ten percent global a newborn and perinatal mortality and mortality [1]. Its mechanism is not readily apparent. Immunologic maladaptation of maternal antibodies to placental and fetal antigens, which may cause inflammation and lead to irregular placentation and placental hypoxia, is another possibility. Vascular sensitivity to angiotensin II is increased, and the production of vasodilators like nitric oxide is reduced which may lead to be the results of placental hypoxia [2].

Risk factors for preeclampsia include hypertension, obesity, nulliparity, chronic diabetes, adolescent pregnancy and conditions leading to hyper placentation and large placentas such as twin pregnancy, renal disease, previous preeclampsia, autoimmune diseases and pregnancies in multiples [3].

Preeclampsia is diagnosed after 20 weeks of gestation. The diagnosis depends on hypertension associated with proteinuria, "Hypertension: systolic blood pressure (SBP)

≥ 140 or diastolic blood pressure (DBP) ≥ 90, proteinuria ≥ 300 mg/24 h. Sever preeclampsia is diagnosed when SBP ≥ 160 or DBP ≥ 110 in addition to one of the six manifestations" [4]. Afamin is a serum glycoprotein that has been proposed as an exact vitamin E binding protein, perhaps accountable for Vitamin E movement in body fluid [5].

In 1994, it was revealed as the 4th member of the albumin superfamily by Lichtenstein et al. Araki *et al.* determined afamin molecular weight as 75000 Dalton. It has been shown to be a precise binding protein for alpha-tocopherol and gamma-tocopherol "two of the most important forms of vitamin E" via multiple binding sites [6]. It is a glycoprotein that is present in biological fluids such as plasma, and cerebrospinal, ovarian follicular and seminal fluids [7]. Albumin, vitamin D binding protein, α-fetoprotein and Afamin belong to the albumin genes family due to the fact that they are on the same chromosome [8]. AFM has an identical amino acid sequence with another albumin family member that is 33% identical to α-fetoprotein (AFP), 29% identical to Albumin and 19% identical to vitamin D binding protein [9].

Afamin, also known as α-albumin, is a liver protein that has a role in antiapoptotic cellular processes linked to oxidative stress (OS). It is a marker for oxidative stress. Insulin resistance (IR) and metabolic syndrome components are related to elevated afamin levels. It may be used as a biomarker to detect abnormal glucose metabolism during pregnancy. In IR, placental mediator release, especially tumornecrosis factore α (aTNF - α), rises in tandem with the severity of the condition. As a result, a high afamin level is linked to poor obstetric outcomes [10].

Material and method

The current study was conducted with 41 patients with preeclampsia (Preeclamptic pregnant women at third trimester) and 30 participants in control group (normal pregnant women at third trimester). Patients' age was ranged between 29.05 ± 0.97 and that of control group ranged between 29.7 ± 1.37. Patients with preterm labor, normal delivery, diabetes mellitus, heart disease, auto-immune disease, renal disease and liver disease were excluded from this study.

Five milliliters (mLs) venous blood had been withdrawn from all pregnant women by the use of disposable syringes in the sitting situation. Then, it was discharged gradually in disposable test tubes without anticoagulant, and kept for clotting at 37 ˚C for 10 to 15 minutes, then centrifugation was applied at 1000 xg for about 10-15 minutes. Their serum was stored in eppendorf tubes at -80 ˚C until analysis of AFM. All participants in this study were selected from Al-Imamain Al-Khadhimain Medical City and asked for their agreement before taking blood samples. The study was ethically approved by the Institutional Review Board (IRB) in College of Medicine/Al-Nahrain University.

Results

The clinical characteristic of the 41 preeclampetic pregnant women and 30 participants in the control group are shown in Table 1. Serum Afamin was significantly greater in patients than that of participants in the control group (Table 2).

TABLE 1 The age of study groups

Characteristic	Control group	All patients	Mild PE	Sever PE	P-value
Number	30	41	18	23	
Age (year)	29.7 ± 1.37	29.05 ± 0.97	27.44 ± 1.63	30.30 ± 1.14	0.697

Data are presented as the means ± SE.

SE, standard error.

TABLE 2 Serum Afamin levels in control and patient groups

Parameter		Mean ± SE	P value Controls vs PE	Controls vs Mild	Controls vs Severe	Mild vs Severe
Serum AFM (ng/mL)	Control	1.63±0.19	0.038	0.022	0.116^{NS}	0.144^{NS}
	PE	2.34±0.23				
	Mild	2.76±0.48				
	Sever	2.00±0.14				

Analysis of variance (*t*-test) showed important differences in the mean of serum AFM between controls vs. total preeclampetic patient group and mild group (0.038 & 0.022). But no significant differences were seen between control group and sever group (0.116) or between mild and sever groups (0.144).

Discussion

The recent study is the first study that evaluates the serum Afamin in pregnant preeclamptic women at third trimester and compared with normal pregnancies. The results of recent study showed that there was no significant difference (P>0.05) in means of maternal age in the cases groups (mild and severe preeclampsia) when compared with normal pregnancies group, also there was no significant difference (P>0.05) between mild and severe preeclampsia groups (Table 1). These findings agreed with those of Nasser NA *et al.* (2020), Tessema *et al*. (2021), and Pihl *et al*. (2020), who presented no differences in mean age of preeclampsia group and control normotensive [11,12,13].

In the current study, the levels of serum afamin were found highly significant in pre-eclamptic pregnant women as compared with the control group. Previous studies found generally that afamin levels did not change between women with poly cystic ovaries (PCOS) and controls but women with insulin resistance (IR) showed higher afamin levels, in any case of the incidence of PCOS [14]. Kollerits *et al*. (2017) found: at baseline, higher levels of Afamin were correlated with prediabetes and T2DM, as well as type 2 diabetes-related phenotypes like IR [15]. Other studies found that pregnancy-related complications such as gestational hypertension GH, preeclampsia PE, intrauterine growth restriction IUGR, preterm birth PB, and gestational diabetes mellitus GDM are linked to afamin [16,17,18, 19].

Conclusion

Serum Afamin levels in the third trimester were not correlated with the severity of preeclampsia in which they decreased in the severe preeclampsia group compared with the serum concentration of mild preeclampsia group but increased when compared with normal pregnant women group.

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