

Article

Assessment of Serum Beta-Catenin, Calcium, and Zinc Levels in Women with Preeclampsia in Baghdad

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Abstract: Preeclampsia is a hypertensive disorder associated with pregnancy and a leading cause of maternal and fetal morbidity and mortality in the world. The pathogenesis of abnormal placentation, endothelial dysfunction, oxidative stress, and inflammatory response has been implicated and is increasingly recognized as playing important roles. The current study was designed to assess the serum level of β -catenin, calcium and zinc in women with preeclampsia and to examine the relationships between β -catenin and lipid profile parameters levels. A case-control study was performed in 60 third trimester pregnant women, 30 women with preeclampsia and 30 healthy pregnant controls. Serum β -catenin was quantified by enzyme-linked immunosorbent assay (ELISA) and calcium, zinc, total cholesterol and triglycerides were assayed by standard biochemical methods. The independent-samples t-test and Pearson's correlation analysis were used to perform the statistical analysis. The results demonstrated that, serum β -catenin, calcium and zinc levels were significantly decreased in women with preeclampsia compared with healthy controls ($P < 0.001$), while the levels of total cholesterol and triglycerides were significantly increased ($P < 0.001$). Moreover, serum β -catenin had significant negative correlations with total cholesterol and triglycerides, as well as positive associations with calcium and zinc levels. No correlation was found between the BMI and β -catenin. The results indicated that decreased serum β -catenin, calcium and zinc levels are correlated with the onset of preeclampsia and may be helpful biochemical markers for the diagnosis of preeclampsia. Larger cohorts are suggested to validate these results and to establish their clinical relevance.

Keywords: Preeclampsia, β -Catenin, Calcium, Zinc, Lipid Profile, ELISA.

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1. Introduction

Preeclampsia is a hypertensive disorder of pregnancy which occurs after 20 weeks gestation, is new onset, and presents with hypertension plus proteinuria or signs of organ dysfunction in mother. One of the top causes of maternal and fetal morbidity and mortality in the world. When preeclampsia becomes severe, blood pressure is significantly high and may be accompanied by liver dysfunction, kidney failure, low platelets, pulmonary edema, neurological and/or visual problems. Untreated, severe preeclampsia can lead to eclampsia, when seizures occur throughout the body and are not caused by other illnesses. [1-4].

The β -catenin protein is a multifunctional protein and is a central player in the Wnt/ β -catenin signaling pathway, which controls cell proliferation, differentiation, migration and placental development. The normal vascularization and the invasion of trophoblast require proper activation of this pathway. Impaired β -catenin signaling has been linked to pregnancy complications such as preeclampsia and eclampsia, and impaired placental function [5].

Furthermore, minerals and trace elements like zinc, calcium, are also important for normal cell function in pregnancy. Zinc serves as an important antioxidant and immune modulator vitamin, whereas calcium plays a role in regulating vascular smooth muscle, neurotransmission and blood pressure. All of these micronutrients have been associated with elevated oxidative stress, endothelial dysfunction, and hypertensive disorders of pregnancy [6, 7].

Although there are many studies exploring the relationship between calcium and zinc with pregnancy complications, there are only few data on the contribution of calcium and zinc to β -catenin in preeclamptic women. The objective of the present study was to assess the serum levels of β -catenin, calcium and zinc in eclamptic women and investigate the role they could play in the pathophysiology of this severe pregnancy complication [8].

1.1 Aim of the Study

The objective of this study was to determine the clinical relevance of levels of serum β -catenin, calcium levels, and zinc levels in women with preeclampsia compared to healthy pregnant women and to test if these levels are associated with the development and severity of preeclampsia.

2. Methods

2.1 Study Design and Subjects

The study was a case-control type study that included 60 pregnant women who were recruited from Al-Imamain Al-Kadhimain Medical City in Baghdad, Iraq. There were two groups for the participants :

Group I (Control group): 30 apparently healthy pregnant women in the third trimester of pregnancy.

Group II (preeclampsia group): 30 pregnant women in the third trimester with a preeclampsia diagnosis by the specialist obstetricians based on strict clinical criteria. Women with chronic systemic diseases, renal, liver, autoimmune or other pregnancy-related complications were not included in the study.

2.2 Collection of samples

Aseptically, 5 mL venous blood was collected from each participant. Blood samples were allowed to coagulate at room temperature and then centrifuged at 3000 rpm for 10 min to get serum. Aliquots of separated serum samples were kept at -20°C until biochemical analysis.

2.3 Biochemical Studies

The concentration of the serum β -catenin was measured by a commercially available enzyme-linked immunosorbent assay (ELISA) kit, following the manufacturer's instructions. Standard colorimetric methods were used for the measurement of serum calcium and zinc concentrations with the use of fully automated clinical chemistry analyser.

2.4 Statistical Analysis

Data was analyzed by using computer software known as Statistical Package for Social Sciences (SPSS) version 26. Data are presented as mean $\pm$ SD. Independent samples t-test was used to determine differences between groups. Correlation analysis was done

between research parameters using Pearson's correlation coefficient and it was considered significant for $p < 0.05$.

3. Results

The results are presented in Table 1 in which the values for biochemical markers obtained from healthy pregnant women (control group) have been compared with those of women with preeclampsia. There was no difference in BMI between the two groups ($P = 0.931$). The total cholesterol and triglyceride levels were significantly higher in the preeclampsia group compared with the control group ($P < 0.001$ for both). Furthermore, PPC women's blood calcium, zinc and β -catenin levels were significantly lower than those of healthy pregnant women ($P < 0.001$ for all parameters). The results suggest that preeclampsia is related with dyslipidaemia, low mineral status and low serum β -catenin levels.

Table 1. Biochemical Parameters Between Healthy Pregnant Women and Women with Preeclampsia

Parameter	Control(mean +SD)	Patients(mean +SD)	P Value
BMI	31.34+ 4.96	31.46+4.30	0.931
Cholesterol mg/dl	153.73+2.92	199.68+2.22	0.000
Triglyceride mg/dl	125.59 +3.030	200.55+ 2.28	0.000
Calcium mg/dl	8.51+0 .40	7.45 +0.64	0.000
Zinc	89.74 + 18.94	66.59 + 9.92	0.000
B- catenin	1.28 +0 .32	0.36 +0.127	0.000

Correlation of Serum β -Catenin Levels with Other Study Parameters

The relationships between serum β -catenin and various biochemical markers measured are displayed in Table 2. There were significant negative correlations between serum β -catenin and total cholesterol ($r = -0.633$, $P < 0.001$) and triglycerides ($r = -0.834$, $P < 0.001$). On the other hand, serum calcium ($r = 0.677$, $P < 0.001$) and serum zinc ($r = 0.650$, $P < 0.001$) were significantly and positively correlated with β -catenin. There was no significant association between β -catenin and BMI ($r = 0.033$, $P = 0.833$). Also, cholesterol and triglycerides were significantly positively correlated. There were negative correlations between both parameters and calcium and zinc concentrations, while the other parameters were not correlated with each other.

Table 2. Correlation Between Serum β -Catenin and Other Study Parameters

Correlations		Bcatenin	CHO	Tri	Ca	Zinc	BMI
Bcatenin	Pearson Correlation	1	-.633**	-.834**	.677**	.650**	.033
	Sig. (2-tailed)		.000	.000	.000	.000	.833
CHO	Pearson Correlation	-.633**	1	.460**	-.523**	-.313*	-.175-
	Sig. (2-tailed)	.000		.002	.000	.038	.255
Tri	Pearson Correlation	-.834**	.460**	1	-.656**	-.555**	.092

	Sig. (2-tailed)	.000	.002		.000	.000	.554
Ca	Pearson Correlation	.677**	-.523**	-.656**	1	.383*	-.088-
	Sig. (2-tailed)	.000	.000	.000		.010	.570
Zinc	Pearson Correlation	.650**	-.313*	-.555**	.383*	1	-.220-
	Sig. (2-tailed)	.000	.038	.000	.010		.152
BMI	Pearson Correlation	.033	-.175-	.092	-.088-	-.220-	1
	Sig. (2-tailed)	.833	.255	.554	.570	.152	
**. Correlation is significant at the 0.01 level (2-tailed).							
*. Correlation is significant at the 0.05 level (2-tailed).							

4. Discussion

In the present study, there was a significant reduction in the serum level of β -catenin in women with preeclampsia when compared to healthy pregnant controls. This information suggests that there is likely to be a defect in Wnt/ β -catenin signalling pathway in preeclamptic pregnancies; β -catenin plays a role in regulating trophoblast cell proliferation, differentiation, migration and placental vascular formation. Decreased β -catenin expression could play a role in a dysfunction of placentation and endothelial function, which are central features of preeclampsia.

Our findings are similar to those of Qin et al. who found lower expression of β -catenin in preeclamptic women's placental tissues and suggested that Wnt/ β -catenin pathway inhibition is associated with abnormal trophoblast invasion and dysfunction of placentas [9].

Similarly, Wang et al. observed that the dysregulation of β -catenin signalling was related with decreased angiogenesis and elevated oxidative stress in preeclamptic placentas [10].

On the other hand, Nusse and Clevers proposed that activation of β -catenin signalling could be a compensatory mechanism in response to cell injury in certain pathological situations of the placenta, such that β -catenin changes could be different depending on the severity of the disease and the tissue type analysed [11].

In the current study, a significant increase in blood cholesterol and triglyceride levels was observed in preeclamptic women. Endothelial dysfunction and oxidative stress in pregnancy are thought to be mostly mediated by maternal dyslipidaemia.

The findings were similar to Spracklen et al. that reported that preeclamptic women had significantly higher levels of cholesterol and triglycerides than normotensive pregnant women [12].

Likewise, Enquobahrie et al. reported a significant link between maternal hypertriglyceridemia and higher risk of preeclampsia, which suggested that abnormal lipid metabolism is a cause of diseases aetiology [13].

On the contrary, Amini et al. showed no significant difference in cholesterol level between mild preeclamptic cases and healthy pregnancies, indicating that the level of severity and gestational age might be the basis for lipid modifications [14].

In the current research, there was considerable decrease in serum calcium in preeclamptic women. Calcium is needed to make blood vessels contract and for blood

pressure. In cases of calcium shortages, more calcium enters the cells of the smooth muscle of blood vessels. This makes the vessels narrow and raises the blood pressure.

This conclusion is in agreement with the work of Jain et al. who observed substantially decreased calcium concentrations in women with preeclampsia as compared to healthy pregnant women [15].

Kisters et al. also reported that calcium deficiency could play a role in the development of increased vascular resistance and hypertension in pregnancy [16].

Sukonpan and Phupong did not find any significant difference in maternal calcium levels in preeclamptic and normotensive pregnancy [17].

In the present study, the serum zinc levels were significantly decreased in preeclamptic women. Zinc is a crucial trace element for antioxidant defence systems and control of inflammatory reactions.

This is in congruence with the study of Ugwuja et al. which found significantly low level of zinc in women with preeclampsia, indicating that zinc deficiency results in oxidative stress and damage to the endothelium [18].

Yart et al. has stated that the poor zinc deficiency may impact the function of placenta [19].

On the other hand, no significant difference was found between preeclampsia and normal pregnancies in zinc levels, as reported by Wang et al. which could be explained by the differences in dietary habits and in the supplementation procedures [20].

The substantial negative association was between β -catenin and cholesterol and triglycerides whereas positive correlation was detected with calcium and zinc levels. The results show that a decrease in β -catenin activity may be related to metabolic abnormalities, endothelial dysfunction and decreased antioxidant defence systems in preeclampsia.

Some of the previous studies indicated that Wnt/ β -catenin signalling is involved in the regulation of lipid metabolism pathways and oxidative stress responses. Thus, the inhibition of β -catenin could be involved in placental dysfunction and systemic metabolic alterations observed in preeclampsia [21, 22].

5. Conclusion

In the present study, serum β -catenin, calcium and zinc were found to be significantly lower in preeclampsia than in healthy pregnant women and serum total cholesterol and triglycerides were found to be significantly higher in preeclampsia than in healthy pregnant women. Moreover, all the parameters of the lipid profile were found to be negatively correlated and calcium and zinc levels are positively correlated with serum β -catenin, indicating that there may be a link between the Wnt/ β -catenin pathway, mineral metabolism, and metabolic disturbances in preeclampsia. The results here suggest that serum β -catenin along with calcium and zinc levels could be used to assess preeclampsia as biochemical markers. However, the results of these studies need to be confirmed by larger multicenter trials and the clinical and diagnostic relevance of these markers needs to be better clarified.

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