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Original Research

Assessment of associations between serum placental leucine aminopeptidase and pregnancy outcomes

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ABSTRACT:

Background: Gestational diabetes mellitus (GDM) and hypertensive disorders of pregnancy (HDP) are common pregnancy complications that can have major effects on both the mother and the fetus. The present study was conducted to assess associations between serum placental leucine aminopeptidase and pregnancy outcomes. **Materials & Methods:**92 women with singleton pregnancieswere divided into 4 groups. Group I were affected by hypertensive disorders of pregnancy (HDP), group II was GDM, group II were of fetal death, and group IV were healthy subjects. Venous blood samples were obtained and measured using L-leucine-p-nitroanilide. **Results:** In group I, II, III and IV, neonatal gender was male in 13, 17, 9, and 10 respectively and female gender in 10, 13, 5 and 13 respectively. The delivery was natural in 14, 18, 14 and 15 and cesarean in 9, 12, 0 and 10 respectively. Apgar score at 1 minute was 8.6, 8.7, 0.0 and 8.2 and at 5 minutes was 9.4, 9.2, 0.0 and 9.7 respectively. The mean serum P-LAP level in group I was 73.2 U/L, in group II was 72.1 U/L, in group III was 4.6 U/L and in group IV was 105.3 U/L. The difference was significant (P< 0.05). **Conclusion:** Serum P-LAP levels were shown to be significantly lower in patients with HDP and GDM as compared to healthy pregnant women, and severely low in patients with fetal mortality. Additionally, low serum P-LAP levels were very sensitive and specific in predicting fetal death.

Keywords: Gestational diabetes mellitus, hypertensive disorders of pregnancy, placental leucine aminopeptidase

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INTRODUCTION

Gestational diabetes mellitus (GDM) and hypertensive disorders of pregnancy (HDP) are common pregnancy complications that can have major effects on both the mother and the fetus. A systolic blood pressure of 140 mm Hg or greater, or a diastolic blood pressure of 90 mm Hg or more, is considered high blood pressure (HDP).[1] It impacts 7%–10% of pregnancies and is a leading cause of illness and death for moms, babies, and fetuses. Pregnancy-induced insulin resistance or glucose intolerance is a characteristic of GDM, which is also linked to detrimental outcomes for mothers and newborns. Maternal hyperglycemia occurs when women without a history of diabetes have elevated blood glucose levels in the third trimester.[2]

The hormone oxytocin is regarded as the most significant uterotonic peptide hormone and plays a crucial part in controlling labor. Only placental leucine aminopeptidase (P-LAP) can break down oxytocin in human serum and the placenta during pregnancy.[3] This cystine aminopeptidase is a member of the M1 family of aminopeptidases, specifically the oxytocinase subfamily. It is membrane-bound in the placenta and usually soluble in mother serum. P-LAP also plays a role in blood pressure regulation, memory retention, antigen presentation, fetal development, and the development of cancer. It also maintains homeostasis throughout pregnancy.[4]

Because P-LAP has been linked to poor outcomes in gynecologic cancers and is involved in regulating tumor cell progression, invasion, and angiogenesis through the degradation or inactivation of peptides like oxytocin, angiotensin, and endothelin-1, it has been suggested that P-LAP could be a viable molecular target in the treatment of gynecologic malignancies. Furthermore, the enzyme P-LAP is exclusive to the placenta.[5]The present study was conducted to assess associations between serum

placental leucine aminopeptidase and pregnancy outcomes.

MATERIALS & METHODS

The present study consisted of 92 women with singleton pregnancies. All gave their written consent to participate in the study.

Data such as name, age, etc. was recorded. They were divided into 4 groups. Group I were affected byhypertensive disorders of pregnancy (HDP), group II was GDM, group II were of fetal death, and group IV were healthy subjects. Venous blood samples were obtained and measured using L-leucine-p-nitroanilide as a substrate in the presence of 20 mM l-methionine. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table I Assessment of parameters

Parameters	Variables	Group I (23)	Group II (30)	Group III (14)	Group IV (25)
Neonatal gender	Male	13	17	9	12
	Female	10	13	5	13
Delivery	Natural	14	18	14	15
	Cesarean	9	12	0	10
Apgar score	1 min	8.6	8.7	0.0	8.2
	5 mins	9.4	9.2	0.0	9.7

Table I shows that in group I, II, III and IV, neonatal gender was male in 13, 17, 9, and 10 respectively and female gender in 10, 13, 5 and 13 respectively. The delivery was natural in 14, 18, 14 and 15 and cesarean in 9, 12, 0 and 10 respectively. Apgar score at 1 minute was 8.6, 8.7, 0.0 and 8.2 and at 5 minutes was 9.4, 9.2, 0.0 and 9.7 respectively.

Table II Assessment of serum P-LAP level

Groups	Mean (U/L)	P value
Group I	73.2	0.01
Group II	72.1	
Group III	4.6	
Group IV	105.3	

Table II, graph I shows that the mean serum P-LAP level in group I was 73.2 U/L, in group II was 72.1 U/L, in group III was 4.6 U/L and in group IV was 105.3 U/L. The difference was significant (P< 0.05).

DISCUSSION

It was previously shown that giving rats with hypertension brought on by renin or angiotensin II will lower their blood pressure.[6] This was achieved by administering pure leucine aminopeptidase derived from the human placenta. It has also been demonstrated that serum P-LAP functions as an angiotensinase by degrading angiotensin III and vasopressin.[7] Numerous aminopeptidases, such as P-LAP, adipocyte-derived leucine aminopeptidase,and aminopeptidase A, have been shown to play important roles in controlling blood pressure in both normal and pathological settings.This data supports the current observation that serum P-LAP levels were significantly lower in HDP patients than in healthy pregnant women.[8] This is not surprising, as low serum P-LAP might raise blood pressure by elevating vasopressin or angiotensin III. However, little research has been done on the mechanisms behind the variations in serum P-LAP levels during pregnancy.[9]Through post-translational splicing, the native membrane-bound form of serum P-LAP may be converted into the soluble form.The length of pregnancy affects serum P-LAP levels, which then decrease following delivery. Through the breakdown of fetoplacental peptides, P-LAP is also probably involved in the development of preterm labor and pre-eclampsia.[10]

We found that in group I, II, III and IV, neonatal gender was male in 13, 17, 9, and 10 respectively and female gender in 10, 13, 5 and 13 respectively. The delivery was natural in 14, 18, 14 and 15 and cesarean in 9, 12, 0 and 10 respectively. Apgar score at 1 minute was 8.6, 8.7, 0.0 and 8.2 and at 5 minutes was 9.4, 9.2, 0.0 and 9.7 respectively.Tian et al[11] examined the relationship between perinatal mortality, gestational diabetes mellitus (GDM), and blood concentrations of placental leucine aminopeptidase (P-LAP) and hypertensive disorders in pregnancy (HDP). Techniques: Between January 2014 and July 2015, women who were healthy and had singleton pregnancies who were afflicted by GDM, HDP, or fetal mortality were included in a prospective study at Shenzhen Seventh People's Hospital in Shenzhen, China. The groups' serum P-LAP concentrations at delivery and at fetal death were contrasted. Serum P-LAP levels' prognostic significance for fetal mortality was assessed. The HDP group (n = 38), GDM group (n = 35), and fetal death group (n = 14) had serum P-LAP concentrations (mean ± SEM) of 74.02 ± 8.45 U/L, 72.57 ± 12.03 U/L, and 3.76 ± 3.02 U/L, respectively, which were all considerably lower than

the meanconcentration of 107.11 ± 30.68 U/L in the control group (n=30; P=0.031, P=0.042, and P=0.001,respectively). On the basis of the receiver operating characteristic curve, low serum P-LAP levels had highsensitivity and specificity for predicting fetal death (100% and 78.9%, respectively, for a serum P-LAP cutoff of47.07 U/L).

We observed that the mean serum P-LAP level in group I was 73.2 U/L, in group II was 72.1 U/L, in group III was 4.6 U/L and in group IV was 105.3 U/L. Yamahara et al[12] in their study P-LAP levels in the placenta and mother's serum were measured during a healthy pregnancy. P-LAP activity in mother serum peaked at 38 weeks of gestation, having increased with gestation to 80 IU/ml. P-LAP mRNA levels in the placenta increased in the third trimester compared to the first, according to northern blot research. The conditioned media of placental tissue contained P-LAP protein and associated activities, whereas the medium of human umbilical vein endothelial cells did not contain them. Throughout the gestation, P-LAP was positively stained by immunohistochemistry in the apical membrane of syncytiotrophoblast cells. These findings, which will be useful to clarify, established the normal range of serum and tissue P-LAP levels during pregnancy as well as the potential source of serum P-LAP.

The limitation of the study is the small sample size.

CONCLUSION

Authors found that serum P-LAP levels were shown to be significantly lower in patients with HDP and GDM as compared to healthy pregnant women, and severely low in patients with fetal mortality. Additionally, low serum P-LAP levels were very sensitive and specific in predicting fetal death.

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