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Original Paper

Association of Polymorphism in Gene of Pregnancy-Associated Plasma Protein A (PAPPA) and Preeclampsia

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ABSTRACT

Background: Preeclampsia is a common disorder of pregnancy. Current study was conducted to determine the association of polymorphism in gene of pregnancy-associated plasma protein A (PAPPA) and preeclampsia. **Methods:** In this prospective cohort study, 134 pregnant women were consecutively enrolled and the blood sampling was performed for genetic analysis in a single lab. Then the subjects were followed-up for preeclampsia and it was seen that 34 women developed preeclampsia and the polymorphism of PAPPA gene was compared between those with and without preeclampsia. **Results:** The results demonstrated that despite twice higher proportion of CC condition of PAPPA in those with preeclampsia in comparison with those with normal pregnancy, there was no significant difference between two groups ($P > 0.05$). **Conclusions:** Totally, according to the obtained results, it may be concluded that polymorphism of pregnancy-associated plasma protein A is not related to occurrence of preeclampsia in pregnant women.

INTRODUCTION

Hypertensive disorders of pregnancy are common in and are responsible for vast majority of morbidities and mortalities beside the bleedings and infections as a triad in pregnancy (1-3). It may be seen in 3.7 percent of cases (4). Nearly 16 percent of deaths due to pregnancy in United States are resulting from hypertension (5). Despite numerous attempts and investigations, the cause of initiation or aggravation of hypertension in pregnancy is not yet clear (2, 3).

Generally, preeclampsia is a pregnancy-specific syndrome of pregnancy with decreased organ perfusion due to vascular spasm and endothelial activation (6). One of the factors proposed to be accompanied with preeclampsia is pregnancy-associated plasma protein A (7, 8). This is a zinc-binding metalloproteinase found firstly in 1974 in pregnant women. It is most prominent index found in pregnancy and the increased levels are seen in hypertension and albuminuria (7, 8). However its role in pregnancy hypertension is controversial and also there are few studies about polymorphism in related gene (9, 10). Hence, current study was conducted to determine the association of polymorphism in gene of pregnancy-associated plasma protein A (PAPPA) and preeclampsia.

METHODS AND MATERIALS

In this prospective cohort study, 134 pregnant women were consecutively enrolled and the blood sampling was performed for genetic analysis in a single lab. Hypertension, preeclampsia, and presence of symptoms such as contractions, vaginal dilatation, PROM, and bleeding were the inclusion criteria. The exclusion criteria were lack of incorporation by patients and impossibility of follow-up.

Then the subjects were followed-up for preeclampsia and it was seen that 34 women developed preeclampsia and the polymorphism of PAPPA gene was compared between those with (n=34) and without preeclampsia (n=100). Also the serum uric acid level, systolic and diastolic blood pressures, and serum creatinine were checked in all patients.

Data analysis was performed among 134 subjects including 100 patients in control group and 34 subjects in case group. Data analysis was performed by SPSS (version 13.0)

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Table 1. Mean laboratory indices

	Creatinine	Platelet	AST	ALT	LDH
Mean	0.79	246941.2	21.4	22.5	206.1
Standard Deviation	0.15	79372.1	9.5	12.6	139.6
Minimum	0.4	123000	9	8	95
Maximum	1.1	477000	48	52	628

Table 2. Frequency distribution of different PAPPA polymorphism in subjects with and without preeclampsia

Group	Type of PAPPA polymorphism			Total
	AA	AC	CC	
Case	6 (17.6%)	17 (50%)	11 (32.4%)	34 (100%)
Control	22 (22%)	62 (62%)	16 (16%)	100 (100%)
Total	28 (20.9%)	79 (59%)	27 (20.1%)	134 (100%)

software [Statistical Procedures for Social Sciences; Chicago, Illinois, USA]. Chi-Square test was used for comparison between groups and was considered statistically significant at P values less than 0.05.

RESULTS

The mean (± standard deviation) age, gravidity, and living child count were 29.88 ± 5.6, 1.82 ± 1.1, and 1.12 ± 0.5, respectively. The age range was from 21 to 45 years. Among the subjects 29.4%, 11.8%, and 8.8% had hypertension, intra-uterine growth retardation, and diabetes mellitus, respectively. The mean laboratory indices are shown in Table 1.

Among the subjects 26.5% had protein in 24-hour urine including 14.75% one-plus, 8.85% two-plus, and 2.9% three plus. However the frequency of CC genotype in case group was two times as this rate in control group (Table 2); there was no significant difference between two groups (P=0.121).

DISCUSSION

To reduce the rate of preeclampsia and prevention of recurrence of this problem in next pregnancies, in this study the association of PAPPA and preeclampsia was evaluated. We found no significant difference between subjects with and without preeclampsia about serum level of PAPPA showing no significant association between PAPPA and preeclampsia. Muravská et al evaluated the association of high-risk pregnancy with preeclampsia, IUGR, preterm labor, and intrahepatic cholestasis and found that TT genotype with Cys327Cys polymorphism was more common in preeclampsia subjects (11).

About the serum level of PAPPA, the evidences are more feasible and some have shown that the low level of PAPPA is accompanied with higher rate of complications during pregnancy especially preeclampsia, low birth weight, and preterm labor (12) and some other studies have reported no significant association (13). Also some studies have reported significant association for some items such as preterm labor and no association for preeclampsia (14). Pilalis et al reported higher prognostic value of simultaneous use of Doppler ultrasonography and PAPPA in comparison with each one separately (15). Such association has been shown for other serum markers such as vitamin D revealing the role of combined markers use a prognostic tool (16).

The study by Ardawi et al showed that smoking and body mass index are related to serum level of PAPPA (17) and these associations should be remembered during statistical analysis to reduce the effect of confounding factors. However in this study none of the subjects were smoker and also regarding some restrictions the body mass index could not be measured. The study by Germanova et al (18) similarly demonstrated no significant association between polymorphism and preeclampsia. This may be due to low power of study and lack of matching between two groups.

The study by Croseley et al (19) revealed that PAPPA-2 subgroup was higher in preeclampsia group in comparison with normotensive pregnant subjects. Their study shows the role of subgroup factors analysis instead total PAPPA measurement. Lower serum level of PAPPA in preeclampsia subjects reported by Spencer et al (20) is also demonstrating the role of subgroups in this era.

Totally, according to the obtained results, it may be concluded that polymorphism of pregnancy-associated plasma protein A is not related to occurrence of preeclampsia in pregnant women. However further studies with larger sample sizes and also control of confounding factors would result in more definite interpretations. Also evaluation of polymorphism in other genes such as those involved in cell transportation of ions such as calcium and magnesium is recommended.

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