

## Placental ADAMTS-5: A new anti-angiogenic protease in the pathogenesis of placenta accreta

Ozler S, Oztas E, Ersoy AO, Caglar T, Celen S, Uygur D, Yucel A, Ergin M, Danisman N  
Zekai Tahir Burak Women's Health Education and Research Hospital, Ankara, Turkey

### Objective

A Disintegrin-like Metalloproteinase with Thrombospondin motif-5 (ADAMTS-5) is an anti-angiogenic and anti-tumorigenic protein and found in the decidua and various fetal tissues in the early stages of embryonic development. In this study, we aimed to determine the placental levels of ADAMTS-5, total antioxidant status (TAS), total oxidant status (TOS), arylesterase and paraoxonase in patients with placenta accreta, placenta previa and in uncomplicated pregnancies.

### Methods

A total of 86 pregnant women were enrolled in this case-control study (27 placenta accreta patients, 29 placenta previa patients without and 30 age-, gestational age- and BMI-matched healthy, uncomplicated pregnant controls). Placental fresh specimens showing no sign of inflammation and/or necrosis macroscopically from the area of the distinct lesion were collected and prominent histological invasion including myometrium were later confirmed. ADAMTS-5, TAS, TOS, paraoxonase and arylesterase level were studied in the placental tissue homogenates. Placental TAS and TOS levels were determined by a novel automated spectrophotometrical method. Paraoxonase and arylesterase activities were measured using commercially available kits and ADAMTS-5 levels in placental tissue were analyzed by ELISA and presented in pg /mg. Determining the best predictor(s) which discriminate placenta accreta was analyzed by multiple logistic regression analyses.

### Results

There were no statistically significant differences among age, gravida, BMI and weight-gain during gestation between groups. There was statistically significant difference among the birth weight of the three groups ( $p < 0.001$ ). The previous history of cesarean section and curettage rates were significantly higher in the accreta group when compared with the other groups ( $p < 0.001$ ). The ADAMTS-5 levels of placenta were distributed as  $41.1 \pm 8.2$  pg/mg in the accreta group,  $59.9 \pm 17.5$  pg/mg in the previa group, and  $60.8 \pm 16.7$  pg/mg in the control group. Among oxidative stress markers in placental tissue only arylesterase levels were significantly lower in the accreta group. ADAMTS-5 levels in the placenta of accreta group were significantly lower than those in the previa and the control groups ( $p < 0.001$ ). ADAMTS-5 levels and both the previous history of cesarean section and curettage were found to be most predictive parameters for the determination of placenta accreta (OR: 1.28 95% CI 1.05-1.559  $P=0.015$ , OR: 1125.5 95% CI: 9.66-131097.15  $P=0.004$  and OR: 13.25 95% CI: 1.37-127.81  $P=0.025$ , respectively).

### Conclusion

Decreased levels of ADAMTS-5 are associated with placenta accreta so we suggest a possible etiological relation between increased angiogenesis due to lower levels of ADAMTS-5 in the occurrence of abnormal placental invasion in patients with placenta previa.

**Table:** Comparison of placental ADAMTS5, TOS, TAS, PON and ARES levels between groups.

	Accreta (n=27)	Totalis (n=29)	Control (n=30)	P value*
ADAMTS-5 (pg/mg)	41.1±8.2	59.9±17.5	60.8±16.7	<0,001*
TOS (nmol H2O2Eq/mg)	5.8±1.8	5.9±1.9	5.5±1.6	0,677
TAS (µmol Trolox Eq/mg)	1.7±0.4	1.7±0.4	1.6±0.3	0,368
Paraoxonase (U/mg)	160.2±57.7	188.9±48.8	191.0±56.4	0,067
Arylesterase (U/mg)	199.1±46.5	254.4±80.8	216.7±49.4	0,004*

\*:  $p < 0.05$  statistically significant, ADAMTS-5: A disintegrin and metalloproteinase with thrombospondin motif 5, TAS: Total antioxidant status, TOS: Total oxidant status.