Oxidative stress biomarkers and ADAMTS-12 levels in early-onset severe preeclampsia and placenta previa

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Objective
Preeclampsia is a unique pregnancy disease characterized by de-novo hypertension and proteinuria after the 20th weeks of gestation. The cause of the disease is still unclear. It is accepted that early-onset (<34th week) preeclampsia is primarily associated with poor, defective placentation due to failure of trophoblastic invasion, whereas late-onset preeclampsia (≥34 weeks) possibly due to a failure of maternal adaptation to pregnancy. Placenta previa (PP) is defined as the implantation of placental tissue somewhere in the lower segment, either over or very close to the internal cervical os. Although the pathogenesis of PP is not known, higher parity, advanced age and previous low segment cesarean section or uterine surgeries are blamed for the higher risk. The fact that both preeclampsia and PP are exceptionally important causes of maternal mortality and morbidity. Interestingly, with unknown reasons, PP is associated with low frequencies of preeclampsia and low maternal blood pressure. We carried out this investigation to address the data about that the risk of preeclampsia is low among pregnant complicated by PP compared with pregnancies in women without PP. Oxidative stress plays many important roles during pregnancy. Reactive oxidative species sometimes harm placental development, but they are also reported to regulate gene transcription and downstream activities such as trophoblastic proliferation, invasion, and angiogenesis. There is evidence that oxidative stress-induced trophoblastic cell dysfunction is one of the major pathology in preeclampsia. Proteases are associated with the process of proteolytic shedding and activation of surface proteins including growth factors, cytokines, receptors and their ligands rather than extracellular matrix breakdown. It has been reported that placental A Disintegrin-like Metalloproteinase with ThromboSpondin motif 12 (ADAMTS-12), independent of its proteolytic activity, plays a specific, non-redundant role in trophoblast invasion. Although oxidative disorders are associated with preeclampsia before, this is the first study to examine the oxidative stress markers and ADAMTS-12 levels in PP. The aim of the present study was to determine whether ADAMTS-12, total oxidant status (TOS), and total antioxidant status (TAS) differ in early onset severe preeclampsia, PP and uncomplicated pregnancies or not.

Methods
The study group consisted of hospitalized and eventually delivered 25 nulliparous pregnant with a diagnosis of early onset severe preeclampsia and 31 nulliparous pregnant with a diagnosis of PP. Thirty-two healthy nulliparous pregnant women without any pregnancy complications and who delivered at ≥37 weeks were recruited within the same time interval as the control group. These cases were collected from a tertiary hospital and met the inclusion criteria for the study. The TOS and TAS of plasma levels were measured using a novel automated colorimetric measurement method. ELISA method was used to determine ADAMTS-12 levels in maternal serum samples.

Results
Women whose pregnancies were complicated with preeclampsia had elevated levels of TOS and TAS when compared with healthy pregnant women (median TOS values: 12.12 and 8.30, P = 0.002; median TAS values: 1.05 and 1.02, P < 0.001, respectively). Serum ADAMTS-12 levels were significantly lower in preeclampsia group when compared with healthy pregnant (p=0.005). There were no significant differences between the preeclampsia and PP groups or between the control and PP groups.

Conclusion
We demonstrated that regardless of the localization the placenta in the uterus, the circulatory biomarkers of oxidative stress and ADAMTS-12 were comparable. The data in this study suggested that the balance between oxidative and antioxidative substances were comparable and normal in pregnancies complicated by PP when compared to normal pregnancies without placentation abnormality. Our data further indicate that the placenta and the fetus of women with PP succeed to reach the increased oxygen demands during pregnancy. In support of this, we encountered no case with preeclampsia and fetal growth restriction in our study groups suggesting normal placental angiogenesis. Contrarily, early onset severe preeclampsia is associated with decreased circulating ADAMTS-12 and increased TOS and TAS levels.