Published in final edited form as:

Am J Reprod Immunol. 2010 December ; 64(6): 376–383. doi:10.1111/j.1600-0897.2010.00861.x.

Maternal Levels of Prostacyclin, Thromboxane, ICAM, and VCAM in Normal and Preeclamptic Pregnancies

David F. Lewis¹, Bernard J. Canzoneri², Yang Gu², Shuang Zhao², and Yuping Wang²

¹Department of Obstetrics and Gynecology, University of Cincinnati, Cincinnati, Ohio

²Department of Obstetrics and Gynecology, Louisiana State University Health Sciences Center – Shreveport, LA, USA

Abstract

Problem—To evaluate whether impaired endothelial function and endothelial inflammatory response occur in parallel in the women with preeclampsia.

Method of Study—Venous blood was drawn from normal ($n = 40$) and severe preeclamptic (sPE) ($n = 40$) pregnant women when they were admitted to the L&D Unit and 24 hrs after delivery. Plasma and serum samples were extracted and measured for 6-keto PGF1 α and TXB₂ (stable metabolites of PGI₂ and TXA₂), and intercellular adhesion molecule (ICAM) and vascular cell adhesion molecule (VCAM) by ELISA. Data are analyzed by Mann–Whitney test and paired t -test. The statistical significance is set as $P < 0.05$.

Results—Plasma 6-keto PGF1 α levels were significantly reduced at admission and 24 hr after delivery in sPE compared to normal pregnant controls, $P < 0.01$. The ratio of 6-keto PGF1 α and TXB₂ was significant less in sPE than that in normal pregnant controls before delivery. There was no significant difference for ICAM and VCAM levels between normal and patients with sPE before and after delivery.

Conclusion—Maternal 6-keto PGF1 α levels and the ratio of 6-keto PGF1 α and TXB₂ were decreased in patients with sPE compared to normal pregnant controls. In contrast, maternal ICAM and VCAM levels were not different between the two groups. These data suggest that serum ICAM and VCAM levels may not be sensitive inflammatory biomarkers for preeclampsia.

Keywords

Intercellular adhesion molecule; preeclampsia; Prostacyclin; thromboxane; vascular cell adhesion molecule

Introduction

Increased vasoconstriction and exaggerated inflammatory response are the two major underlying pathophysiological characteristics in the maternal systemic vasculature in preeclampsia.^{1,2} The marked increase in the vascular peripheral resistance contributes to the maternal hypertension. In terms of vasoactivators, it is well known that vascular endothelium is the main source of prostacyclin (PGI₂) and nitric oxide (NO), which play an important role in vasculature relaxation. PGI₂, especially, is a potent vasodilator and an

inhibitor of platelet aggregation. In contrast, thromboxane A₂ (TXA₂), which results from the degranulation of platelets upon activation, is a potent vasoconstrictor as well as a platelet aggregator. In normal pregnancy, delicate balance exists between vasodilators and vasoconstrictors to maintain a normal vasomotor tone and vasoactivity. Whereas during preeclampsia, decreased PGI₂ levels and/or increased TX levels or the imbalance of PGI₂ to TX contribute significantly to the increased vasoconstriction in both the maternal systemic and the placental vasculatures. In preeclampsia, maternal vessels also display structural changes.^{3,4} For example, Svedas et al.³ observed that endothelial cells were shrunk with blebbing, and thin plasma membranes detached from basal lamina in myometrial artery vessels from preeclampsia. These arteries were noted to have reduced bradykinin-mediated dilatory response, confirming impaired vasodilatation in the vessels from women with preeclampsia.

Exaggerated inflammatory responses are also believed to be a significant pathophysiological event during preeclampsia.⁵ Several biochemical parameters indicate that endothelial dysfunction is related to the inflammatory response in preeclampsia, such as elevated serum cellular fibronectin levels^{6,7} and increased endothelial adhesion molecules P-selectin, intercellular adhesion molecule (ICAM), vascular cell adhesion molecule (VCAM), and platelet endothelial cell adhesion molecule (PECAM).⁸⁻¹¹ These measurable soluble molecules have been considered as biomarkers to monitor endothelial function in preeclampsia.^{5,8,9}

Both decreased vasodilator PGI₂ levels and increased soluble endothelial adhesion molecule levels are linked to endothelial dysfunction during preeclampsia. Although many studies have shown decreased PGI₂ with or without increased TX levels, as well as altered endothelial adhesion molecule levels in women with preeclampsia compared to those from normal pregnant women, it is not known whether the two events, impaired endothelial vasodilator production and endothelial activation resulting in increased endothelial adhesion molecule expression/release, occur in parallel in the maternal system in women with preeclampsia. To test this, in this study, we measured plasma vasodilator PGI₂ levels as an indicator of endothelial ability to respond vasoconstriction and serum soluble ICAM and VCAM levels as indicators of endothelial inflammatory response in women with preeclampsia. We then compared the levels with those levels in women with normal pregnancy. We also measured vasoconstrictor TX levels as a comparison to PGI₂. We hypothesized that the two events may occur simultaneously in the maternal system during preeclampsia.

Materials and methods

Sample Collection and Patient Information

This study was approved by the Institutional Review Board (IRB) for Human Research at Louisiana State University Health Sciences Center – Shreveport (LSUHSC-S), LA. Patients, women diagnosed with normal pregnancy and severe preeclampsia, were recruited when they were admitted to the Labor and Delivery Unit at LSUHSC-S from January 2003 to December 2005. Written consent was obtained. Normal pregnancy is defined as pregnancy with normal blood pressure (<140/90 mmHg), no proteinuria, and absence of obstetrical and medical complications. Diagnosis of severe preeclampsia is defined as ACOG Practice Bulletin¹²: sustained systolic blood pressure of ≥160 mmHg or a sustained diastolic blood pressure of ≥110 mmHg; proteinuria measurement of 3+ or more on dipstick, or 24-hr urine protein collection with ≥5 g in specimen; urine output <30 mL per hour for 2 hr unresponsive to 500 mL intravenous fluid challenge; presence of persistent headache, and visual disturbances, or epigastric pain; patients with one or more abnormal laboratory values reflecting thrombocytopenia, elevated LDH or increased aspartate aminotransferase;

pulmonary edema or evidence of intrauterine growth restriction. Each patient had two venous blood draws, one at admission before medication and one at 24 hr post-partum. Aliquot plasma and serum samples were stored in -70°C .

Measurement of Prostacyclin and Thromboxane

Plasma levels of PGI_2 and TXA_2 were measured by their stable metabolites of 6-keto-PGF 1α and TXB_2 by enzyme-linked immunosorbent assay (ELISA). Both 6-keto-PGF 1α and TXB_2 ELISA kits were purchased from Oxford Biomedical Research, Inc. (Oxford, MI, USA). Plasma samples for measurements of 6-keto-PGF 1α and TXB_2 were extracted by C18 Sep-Pak column (Waters Corporation, Milford, MA, USA) following the standard manufacture instruction before assay. Briefly, 0.2 mL of methanol was added to 1.0 mL of plasma sample and mixed well, and then the mixture was applied into a C18 Sep-Pak column with flow rate to 1.0 mL per minute. The C18 Sep-Pak column was preconditioned with 2.0 mL of 100% methanol and 2.0 mL of double distilled H_2O . After the plasma/methanol mixture passed the column, the column was washed with 2.0 mL of 15% methanol followed by 2.0 mL of petroleum ether. The 6-keto-PGF 1α and TXB_2 sample was eluted by 2.0 mL of methyl formate, which was evaporated by nitrogen gas. The residue was diluted with 1.0 mL of extraction buffer provided by the ELISA kit.

The assay was performed in a 96-well ELISA plate. The ELISA kit includes ELISA buffer, washing buffer, extraction buffer, substrate, standard enzyme conjugate, and antibody-coated plate. The standard curve for 6-keto-PGF 1α had a range of 20–200 pg/mL. The standard curve for TXB_2 had a range of 4–400 pg/mL. An aliquot of 50 μL per sample was assayed in duplicate for both 6-keto-PGF 1α and TXB_2 ELISA assays. Within- and between-assay variations were less than 8%.

Measurement of ICAM and VCAM

Maternal serum levels for ICAM and VCAM were measured by enzyme-linked immunosorbent assay (ELISA). The DuoSet ELISA Development kit for both ICAM and VCAM kits were purchased from R&D systems (R&D systems, Minneapolis, MN, USA). The range of the standard curve was 31.25–2000 pg/mL for both ICAM and VCAM assays. All samples were measured in duplicate. Within- and between-assay variations were less than 7%. Assays were performed according to the manufacturers' instruction.

Statistical Analysis

Demographic and clinical data are presented as mean $\pm$ S.D. (Tables I and II). Data for 6-keto-PGF 1α , TXB_2 , ICAM, and VCAM are presented as mean $\pm$ S.E. and analyzed by Mann–Whitney test or student *t*-test for comparison between normal and preeclamptic groups. Paired *t*-test was used for analysis of 6-keto-PGF 1α , TXB_2 , ICAM, and VCAM data in normal and preeclamptic groups before and after delivery. Simple regression was used to analyze regression coefficients between platelet counts and maternal TXB_2 levels at admission in women with preeclampsia. Computer software STATVIEW (SAS Institute, Inc. Cary NC, USA) was used. The statistical significance is defined as $P < 0.05$. Power analysis was performed by a computer program Power and Precision (Biostat, Englewood, NJ, USA). Based on admission 6-keto-PGF 1α levels, it needs 32 patients in each arm to achieve 80% power level, i.e., $\alpha = 0.05$, 2-tailed, and power = 0.80. In this study, we included 40 patients (25% more patients) in each arm to minimize patient selection bias.

Results

Patient Clinical Data

A total of eighty pregnant patients were included in this study, forty with normal pregnancy and forty with severe preeclampsia. The clinical characteristics of the study population for normal and preeclamptic pregnancies are shown in Table I. There are no statistical differences for maternal age and primigravida between normal and preeclamptic groups. Gestational age was significantly less, and systolic/diastolic blood pressure was significantly higher in the preeclamptic group than in the normal pregnant group. Table II presents maternal blood pressures, platelet counts and hematocrits at admission, and MgSO_4 concentrations 2 hr after initial bolus infusion and 24 hr post-partum for preeclamptic patients. Maternal blood pressure and hematocrit were significantly reduced 24 hr after delivery. There was no difference for platelet counts at admission and blood MgSO_4 levels 2 hr after initial bolus infusion and 24 hr after delivery. None of patients with preeclamptic has HELLP syndrome.

Maternal Levels for 6-keto $\text{PGF1}\alpha$ and TXB_2

The maternal 6-keto $\text{PGF1}\alpha$ and TXB_2 levels at admission and 24 hr post-partum are presented in Table III. Maternal 6-keto $\text{PGF1}\alpha$ levels are significantly reduced in women with preeclampsia compared to those in women with normal pregnancies at admission and at 24 hr after delivery; admission: 158.01 ± 15.20 versus 254.51 ± 27.31 pg/mL, $P < 0.01$; 24 hr post-partum: 144.37 ± 21.90 pg/mL versus 225.41 ± 24.25 pg/mL, $P < 0.01$. In contrast, there is no difference for TXB_2 levels at admission between preeclamptic and normal pregnant women, 41.28 ± 8.42 pg/mL versus 46.36 ± 4.23 pg/mL. The TXB_2 levels are reduced in patients with preeclampsia 24 hr after delivery compared to those in normal pregnant controls, 31.74 ± 6.16 versus 49.10 ± 7.15 pg/mL, $P < 0.05$, respectively. Maternal levels of 6-keto $\text{PGF1}\alpha$ and TXB_2 are not different between admission and 24 hr after delivery in normal pregnant controls (Table III).

The ratio of 6-keto- $\text{PGF1}\alpha$ to TXB_2 is significantly less in preeclampsia at admission, 5.05 ± 0.55 , compared to that in normal pregnant controls, 7.21 ± 0.91 , $P < 0.05$. The ratio for 6-keto- $\text{PGF1}\alpha$ to TXB_2 is approximately 25% increased at 24 hr post-partum compared to that before delivery in women with preeclampsia. There is no statistical difference for the ratio of 6-keto- $\text{PGF1}\alpha$ / TXB_2 at 24 hr postpartum between preeclampsia and normal pregnant controls, 6.33 ± 1.01 versus 7.75 ± 1.16 (Table III).

Maternal Levels for ICAM and VCAM

Maternal serum levels for ICAM and VCAM at admission and 24 hr post-partum in normal pregnancies and pregnancies complicated by preeclampsia are shown in Table IV. There is no significant difference for ICAM and VCAM levels both at admission and 24 hr post-partum between normal pregnancy and preeclampsia.

Correlation Between the Platelet Count and the TXB_2 Concentration in Preeclampsia

As thromboxane is released by circulating platelets, a correlation analysis was done on the relationship between the platelet count and the maternal plasma level of TXB_2 at admission in women with preeclampsia. No significant positive correlation was revealed between the maternal platelet count and the maternal plasma TXB_2 as presented in Fig. 1.

Discussion

In this study, we evaluated 6-keto- $\text{PGF1}\alpha$, TXB_2 , ICAM, and VCAM levels in the maternal blood samples obtained from normal and preeclamptic pregnant women at admission to

Labor and Delivery and 24 hr after delivery. 6-keto-PGF1 α and TXB₂ were used as the indicators of vasoactivity. ICAM and VCAM were used as indicators of endothelial inflammatory response. We wanted to learn whether their level changes were concomitantly or in parallel before and after delivery, and what the difference was between normal pregnancy and preeclampsia.

Our results showed that the levels for 6-keto PGF1 α are significantly less in plasma samples from women with preeclampsia than those from normal pregnant controls both at the admission and 24 hr post-partum. There is no significant difference in TXB₂ levels between normal and preeclamptic pregnancies at admission, but the TXB₂ levels are decreased in preeclamptic pregnancies 24 hr after delivery. Although no changes were noticed for TXB₂ levels in normal pregnant women between admission and 24 hr after delivery, the results show a 25% reduction in the ratio of 6-keto PGF1 α to TXB₂ in patients with preeclampsia at admission compared to that in normal pregnant controls. These results are consistent with previously published works,^{13,14} indicating the balance between PGI₂ and TXA₂ favors to TX₂ in preeclampsia. The disproportion between PGI₂ and TXA₂ is believed to contribute to the increased vasoconstriction in preeclampsia.¹³ Furthermore, the reduced PGI₂/TXA₂ ratio reflects endothelial cell dysfunction, which is unable to properly generate PGI₂ to compensate the increased vasoconstrictive state during preeclampsia. In fact, the reduced maternal-circulating PGI₂/TXA₂ ratio is in line with the imbalance of placental production between prostacyclin and thromboxane previously found in preeclampsia.^{15,16} It is believed that this reduced ratio represents the upcoming overt clinical symptoms characterized by vasoconstriction and portends the development of preeclampsia.¹⁷ With the imbalance between prostacyclin and thromboxane in favor of thromboxane, the biological action of thromboxane on constricting vasculature can be taken into effect in addition to the reduced vasodilatory effect by endothelial prostacyclin. The PGI₂/TXA₂ ratio is increased by 25% approximately 24 hr after delivery in women with preeclampsia, suggesting that there is an elevated level of PGI₂ within 24 hr post-partum, which parallels a reduction in blood pressure and an improved clinical condition in preeclamptic patients. Thus, in spite of the absolute value of either PGI₂ or TXA₂ within the maternal circulation, the reduced PGI₂/TXA₂ ratio is a reliable factor for potential vasoconstriction characterizing endothelial dysfunction in preeclampsia.

Previously published works showed that ICAM and VCAM levels were either elevated^{8,9} or no difference¹⁸ in patients with preeclampsia compared to normal pregnant controls. In this study, we found no difference for ICAM and VCAM levels at admission and 24 hr after delivery between normal pregnancy and preeclampsia in our patient population. The exact mechanism for the regulation of CAM within the circulation in preeclampsia is not clear. Marks et al.¹⁹ measured ICAM, VCAM, and E-selectin levels in pregnant women living high altitude. They found that serum levels of these adhesion molecules were not significantly different from those living at the sea level. Their data suggest that maternal systemic hypoxia is not responsible for this pathway of endothelial cell activation in preeclampsia.¹⁹ Alternatively, it was suggested that the plasma level of TX might be a regulatory/contributing factor in the expression of cell adhesion molecules. For example, an animal study showed that TX generated from the activated platelets promotes ICAM and VCAM upregulation on endothelial cells.²⁰ Cell culture experiments also found that TXA₂ inhibitor suppressed ICAM expression on activated endothelial cells while TXA₂ agonists augmented the endothelial VCAM expression.²¹ Thus, plasma TX level might be causally linked to the circulating ICAM and VCAM levels. This might explain the results in our study with the TX level in preeclampsia that was compatible with that of the normal pregnancy, in which the soluble ICAM and VCAM also showed no significant difference before delivery and 24 hr post-partum. Another explanation could be because of the labor-induced effects. It was reported that the ripening of the cervix during labor is a pro-

inflammatory reaction, leading to the upregulation of certain cell adhesion molecules within the cervix and the lower uterine segment,^{22,23} but it is not known whether the local upregulated cell adhesion molecules in the cervix and the lower uterine segment could contribute to the elevated circulating soluble cell adhesion molecule levels. In our patient setting, although there were about 2/3 patients in the normal pregnant group and 1/3 in the preeclamptic group who had vaginal delivery, we did not notice any difference in ICAM and VCAM levels associated with delivery mode. Thus, it is unlikely that the difference in sICAM and sVCAM levels between preeclampsia and normal pregnancy could be masked by the intra-partum elevation of these molecules during active labor in some of normal controls.

It has been shown that with the absence of upregulated endothelial expression of ICAM and VCAM, the circulating pro-inflammatory cytokines such as TNF α are unable to trigger the aggregation of leukocytes and platelets, which is the pre-requisite for the endothelial phenotypic transformation to the proinflammatory and pro-thrombotic one.²⁴ Thus, elevated levels of these soluble cell adhesion molecules might be the more specific indicator for the endothelial inflammatory response *per se*. Once initiated, activated endothelium activates leukocytes and/or *vice versa* in the process of inflammation within the circulation.²⁵ In the case of preeclampsia, both the endothelial activation/dysfunction and amplified activation of the circulating components have been demonstrated.^{5,26} However, it is not known whether the earlier changes in the preeclamptic state are leukocytic or endothelial. It is very likely that the altered endothelial function is an earlier event. Furthermore, results from this study suggest that among the consequences of endothelial activation/dysfunction responses, reduced vasodilator production of PGI₂ by vascular endothelium or failure of adaptation to increased vasoconstrictive activity might occur prior to the enhanced endothelial inflammatory response during preeclampsia.

All the patients in preeclamptic group were administrated with magnesium sulfate. However, the 6-keto PGF1 α data suggest that magnesium sulfate do not affect maternal PGI₂ levels (Table II). We believe that the changes in PGI₂ levels before and after delivery further indicate the important compensatory effects of this vasodilation agent on the physiological adaptation to the increased blood volume and reduced vascular resistance during pregnancy. Increased TX levels in the maternal circulation have been reported in women with preeclampsia compared to that in women with normal pregnancies.¹³ Platelets are a major source of thromboxane in the systemic circulation, however, this study did not detect difference in TX levels at admission between preeclamptic pregnancies and their normal controls. The relatively stable platelet count in the study patients (Table II) could, at least in part, explain the phenomena of compatible TX levels between normal and preeclamptic pregnancies. In comparison, we did observe a reduction in TX levels 24 hr after delivery in women with preeclampsia. In this study, most patients with preeclampsia were delivered before 34 weeks of gestation, and they usually received steroids 48 hr before termination of pregnancy to promote fetal lung maturity. Both magnesium and steroids exert platelet inhibitory function.^{27,28} Therefore, inhibition of platelet activation and aggregation by magnesium and steroids could protect platelets from degranulation and TX release. This could be a reason for reduced TXB₂ levels seen in post-partum samples from patients with preeclampsia.

In conclusion, we found that maternal 6-keto-PGF1 α levels and the ratio of 6-keto-PGF1 α /TXB₂ were reduced in patients with preeclampsia compared to normal pregnant patients. We did not detect any difference for ICAM and VCAM levels between normal and preeclamptic pregnancies in our study population. This data suggest that serum ICAM and VCAM levels may not be sensitive inflammatory biomarkers for preeclampsia. It is likely that diverse regulatory mechanisms exist for prostacyclin production and ICAM and VCAM

shedding from vascular endothelium, although altered vasoactivators and increased adhesion molecule levels may have the common “read out” once terminal stage has been reached.²⁶

Acknowledgments

This study was supported in part by grants from National Institute of Health, National Institute of Child Health Development (HD36822), and National Heart Blood Lung Institute (HL65997).

References

1. Lindheimer, MD.; Roberts, JM.; Cunningham, FC. Chesley's Hypertensive Disorders in Pregnancy. 2nd edn. Stamford, Connecticut: Appleton & Lange; 1999.
2. Roberts JM, Taylor RN, Musci TJ, Rodgers GM, Hubel CA, McLaughlin MK. Preeclampsia: an endothelial cell disorder. *Am J Obstet Gynecol.* 1989; 161:1200–1204. [PubMed: 2589440]
3. Svedas E, Nisell H, Vanwijk MJ, Nikas Y, Kublickiene KR. Endothelial dysfunction in uterine circulation in preeclampsia: Can estrogens improve it? *Am J Obstet Gynecol.* 2002; 187:1608–1616. [PubMed: 12501072]
4. Svedas E, Islam KB, Nisell H, Kublickiene KR. Vascular endothelial growth factor induced functional and morphologic signs of endothelial dysfunction in isolated arteries from normal pregnant women. *Am J Obstet Gynecol.* 2003; 188:168–176. [PubMed: 12548213]
5. Redman CWG, Sacks GP, Sargent IL. Preeclampsia: An excessive maternal inflammatory response to pregnancy. *Am J Obstet Gynecol.* 1999; 180:499–506. [PubMed: 9988826]
6. Friedman SA, de Groot CJM, Taylor RN, Golditch BD, Roberts JM. Plasma cellular fibronectin as a measure of endothelial involvement in preeclampsia and intrauterine growth retardation. *Am J Obstet Gynecol.* 1994; 170:838–841. [PubMed: 8141213]
7. Taylor RN, Crombleholme WR, Friedman SA, Jones LA, Casal DC, Roberts JM. High plasma cellular fibronectin levels correlate with biochemical and clinical features of preeclampsia but cannot be attributed to hypertension alone. *Am J Obstet Gynecol.* 1991; 165:895–901. [PubMed: 1951550]
8. Krauss T, Kuhn W, Lakoma C, Augustin HG. Circulating endothelial cell adhesion molecules as diagnostic markers for the early identification of pregnant women at risk for development of preeclampsia. *Am J Obstet Gynecol.* 1997; 177:443–449. [PubMed: 9290466]
9. Lyall F, Greer IA, Boswell F, Macara LM, Walker JJ, Kingdom JCP. The cell adhesion molecule, VCAM-1, is selectively elevated in serum in pre-eclampsia: does this indicate the mechanism of leucocyte activation? *Br J Obstet Gynaecol.* 1994; 101:485–487. [PubMed: 7517182]
10. Wang Y, Lewis DF, Groome L, Zhang Y, Gu Y, Philibert L. Enhanced P-selectin expression in the maternal vessel endothelium and elevated soluble P-selectin levels in the maternal plasma in women with preeclampsia. *J Soc Gynecol Investig.* 2005; 12:276A.
11. Austgulen R, Lien E, Vince G, Redman CWG. Increased maternal plasma levels of soluble adhesion molecules (ICAM-1, VCAM-1, E-selectin) in preeclampsia. *Eur J Obstet Gynecol Reprod Biol.* 1997; 71:53–58. [PubMed: 9031960]
12. ACOG Practice Bulletin: Diagnosis and management of preeclampsia and eclampsia. Number 33. *Obstet Gynecol.* 2002; 99:159–167. [PubMed: 16175681]
13. Wang Y, Walsh SW, Guo J, Zhang J. The imbalance between thromboxane and prostacyclin in preeclampsia is associated with an imbalance between lipid peroxides and vitamin E in maternal blood. *Am J Obstet Gynecol.* 1991; 165:1695–1700. [PubMed: 1750462]
14. Goeschen K, Henkel E, Behrens O. Plasma prostacyclin and thromboxane concentrations in 160 normotensive, hypotensive, and preeclamptic patients during pregnancy, delivery, and the post partum period. *J Perinat Med.* 1993; 21:481–489. [PubMed: 8006773]
15. Walsh SW. Preeclampsia: An imbalance in placental prostacyclin and thromboxane production. *Am J Obstet Gynecol.* 1985; 152:335–340. [PubMed: 3923838]
16. Walsh SW, Wang Y. Trophoblast and placental villous core production of lipid peroxides, thromboxane, and prostacyclin in preeclampsia. *J Clin Endocrinol Metab.* 1995; 80:1888–1893. [PubMed: 7775637]

17. Chavarria ME, Lara-Gonzalez L, Gonzalez-Gleason A, Garcia-Paleta Y, Vital-Reyes VS, Reyes A. Prostacyclin/thromboxane early changes in pregnancies that are complicated by preeclampsia. *Am J Obstet Gynecol.* 2003; 188:986–992. [PubMed: 12712098]
18. Lyall F, Hayman RG, Ashworth JR, Duffie E, Baker PN. Relationship of cell adhesion molecule expression to endothelium-dependent relaxation in normal pregnancy and pregnancies complicated with preeclampsia or fetal growth restriction. *J Soc Gynecol Investig.* 1999; 6:196–201.
19. Marks L, Zamudio S, Cousins F, Duffie E, Lyall F. Endothelial activation and cell adhesion molecule concentrations in pregnant women living at high altitude. *J Soc Gynecol Investig.* 2006; 13:399–403.
20. Mitsuhashi M, Tanaka A, Fujisawa C, Kawamoto K, Itakura A, Takaku M, Hironaka T, Sawada S, Matsuda H. Necessity of thromboxane A2 for initiation of platelet-mediated contact sensitivity: dual activation of platelets and vascular endothelial cells. *J Immunol.* 2001; 166:617–623. [PubMed: 11123345]
21. Ishizuka T, Suzuki K, Kawakami M, Hidaka T, Matsuki Y, Nakamura H. Thromboxane A2 receptor blockade suppresses intercellular adhesion molecule-1 expression by stimulated vascular endothelial cells. *Eur J Pharmacol.* 1996; 312:367–377. [PubMed: 8894620]
22. Osman I, Crawford M, Jordan F, Young A, Norman J, Thomson A. Expression and localization of cell adhesion molecules in human fetal membranes during parturition. *J Reprod Immunol.* 2004; 63:11–21. [PubMed: 15284000]
23. Winkler M, Kemp B, Fischer DC, Ruck P, Rath W. Expression of adhesion molecules in the lower uterine segment during term and preterm parturition. *Microsc Res Tech.* 2003; 60:430–444. [PubMed: 12567400]
24. He P, Zhang H, Zhu L, Jiang Y, Zhou X. Leukocyte-platelet aggregate adhesion and vascular permeability in intact microvessels: role of activated endothelial cells. *Am J Physiol Heart Circ Physiol.* 2006; 291:H591–H599. [PubMed: 16517944]
25. Mesri M, Altieri DC. Leukocyte microparticles stimulate endothelial cell cytokine release and tissue factor induction in a JNK1 signaling pathway. *J Biol Chem.* 1999; 274:23111–23118. [PubMed: 10438480]
26. Roberts JM, Lain KY. Recent Insights into the pathogenesis of pre-eclampsia. *Placenta.* 2002; 23(5):359–372. [PubMed: 12061851]
27. Ravn HB, Vissinger H, Kristensen SD, Husted SE. Magnesium inhibits platelet activity—an in vitro study. *Thromb Haemost.* 1996; 76:88–93. [PubMed: 8819258]
28. Sheu JR, Hsiao G, Shen MY, Fong TH, Chen YW, Lin CH, Chou DS. Mechanisms involved in the antiplatelet activity of magnesium in human platelets. *Br J Haematol.* 2002; 119:1033–1041. [PubMed: 12472585]

Fig. 1. Correlation of plasma TXB₂ concentration with platelet counts at admission in women with preeclampsia. There was no significant correlation of plasma TXB₂ levels with platelet counts: $y = 0.000x + 0.013$, $r = 0.203$.

Table I

Demographic Data for Study Subjects

	Normal Pregnancy (n = 40)	Preeclampsia (n = 40)	P value
Maternal age ^a	22 ± 3	24 ± 6	>0.5
Racial status			
Black	35	24	–
White	4	15	–
Other	1	1	–
Gestational age ^a	40 ± 1	34 ± 4	<0.0001
Primigravida (%)	45%	51%	–
Blood pressure ^a			
Systolic	125 ± 10	166 ± 17	<0.0001
Diastolic	67 ± 12	102 ± 13	<0.0001
Mode of delivery			
Vaginal delivery	28	15	–
Cesarean section	12	25	–

^aData are presented as mean ± S.D.

Table II

Maternal Blood Pressures, Platelet Counts, Hematocrits, and MgSO₄ Concentrations at Admission and 24 hr Post-partum in Women Complicated by Preeclampsia

	Admission	24 hr post-partum	<i>P</i> value
Blood pressure (mmHg)			
Systolic BP	166 ± 17	144 ± 15	<0.0001
Diastolic BP	102 ± 13	84 ± 10	<0.0001
Platelets (10 ³ /μL)	224 ± 57	216 ± 60	0.270
Hematocrit (%)	34.03 ± 4.08	29.55 ± 4.97	<0.0001
MgSO ₄ concentration (mg/dL)	3.64 ± 1.16 ^a	4.13 ± 1.70	0.245

Data are presented as mean ± S.D.

^a 2 hr after the bolus infusion.

Maternal Plasma Levels for 6-keto PGF1 α and TXB₂ at Admission and 24 hr Post-Partum in Normal Pregnant Women and in Women Complicated by Preeclampsia

Table III

	6-keto PGF1 α (pg/mL)		TXB ₂ (pg/mL)		6K/1X Ratio	
	Admission	24 hr PP	Admission	24 hr PP	Admission	24 hr PP
Nor-Pregnancies	254.51 $\pm$ 27.31	225.41 $\pm$ 24.25	46.36 $\pm$ 4.23	49.10 $\pm$ 7.15	7.21 $\pm$ 0.91	7.75 $\pm$ 1.16
Preeclampsia	158.01 $\pm$ 15.20**	144.37 $\pm$ 21.90**	41.28 $\pm$ 8.42	31.74 $\pm$ 6.16*	5.05 $\pm$ 0.55*	6.33 $\pm$ 1.01

Data are presented as mean $\pm$ S.E.
Preeclampsia vs. normal pregnancies:
* $P < 0.05$;
** $P < 0.01$.

Table IV

Maternal Serum Levels for sICAM and sVCAM at Admission and 24 hr Post-partum in Women with Normal Pregnancies and in Women Complicated by Preeclampsia

	ICAM (ng/mL)		VCAM (ng/mL)	
	Admission	24 hr PP	Admission	24 hr PP
Nor-Pregnancies	169.01 ± 6.71	167.10 ± 8.03	307.90 ± 10.15	307.86 ± 10.43
Preeclampsia	174.96 ± 14.35	174.20 ± 13.26	322.76 ± 12.62	305.09 ± 12.10

Data are presented as mean ± S.E.

PP, post-partum; ICAM, intercellular adhesion molecule; VCAM, vascular cell adhesion molecule.