International Journal of
Health Systems and Medical Science

ISSN: 2833-7433
Volume 1 | No 4 | Oct-2022

New Indicators of Endothelial Dysfunction - Predictors of Recurrent Obstetric Bleeding

Usmanova N. Yu. [1], **Karimova N. N.** [2]

[1, 2] Republican Scientific Center of Emergency Medical Care Bukhara branch, Uzbekistan

Abstract: The main indicators of endothelial dysfunction are endothelin-1 (ET-1), nitric oxide (NO), E-selectin and vascular endothelial growth factor (VEGF). The clinical course of the present pregnancy was studied in 32 of 53 examined pregnant women who had a history of massive bleeding, proceeded without complications, and in 38 pregnant women the threat of miscarriage was revealed. In this regard, we decided to divide them into 2 groups: without the threat of miscarriage, with the threat of miscarriage. An individual analysis of the indicators of endothelial dysfunction showed a pronounced dysfunctional state in pregnant women of the group at risk of miscarriage. Revealed at 18-24 weeks of pregnancy in the blood serum of pregnant women without signs of miscarriage, an increase in the level of ET-1, NO, E-selectin and VEGF was revealed by 1.66; 1.2; 1.32 and 1.17 times relative to the indicators of women with the physiological course of pregnancy. In pregnant women with the threat of miscarriage, this excess was 3.33; 1.59; 1.72 and 1.68 times, respectively. It should be said that in this group of pregnant women the level of ET-1, NO, E-selectin and VEGF in 2; 1.32; 1.31 and 1.44 times the values of pregnant women without the threat of miscarriage.

Keywords: massive obstetric bleeding, operations, endothelial dysfunction, endothelin-1, nitric oxide, selectin, growth factor, preeclampsia, miscarriage.

Conduction. Recently, vascular endothelium plays a very important role in the development of vascular disorders. It performs barrier, secretory, hemostatic, vasotonic functions (1,2,3). In many pathological conditions, including complicated pregnancy, the endothelium reacts to various humoral changes in the internal environment by producing vasoconstrictor and vasodilator factors, adhesion molecules, the balance of which determines the tone of smooth muscle cells, being very important in the regulation of vascular tone. Among the numerous factors of endothelial origin, the recognized markers of endothelial dysfunction are nitric oxide (NO) and angiotensin converting enzyme (5,6). In addition, in recent years, great importance has been attached to the development of endothelial dysfunction by endothelin, which is able to influence changes in vascular tone both directly and indirectly through the generation of nitric oxide and the formation of angiotensin II. The main indicators of endothelial dysfunction are endothelin-1 (ET-1), nitric oxide (NO), E-selectin and vascular endothelial growth factor (VEGF) (5,7). However, it should be said that the values of pregnant women varied widely. Therefore, we decided to analyze the results obtained individually for each pregnant woman, taking into account the presence of obstetric complications of this pregnancy.

The purpose of the study. Identification of new indicators of endothelial dysfunction as predictors of recurrent obstetric bleeding.

Results and discussion. Studies have shown that pregnant women who have had a history of massive bleeding, at 18-24 weeks of pregnancy, serum levels of ET-1, NO, E-selectin and VEGF increased by 2.33 ($P<0.001$); 1.2 ($P>0.05$); 1.48 ($P<0.05$) and 1.37 ($P<0.01$) times relative to the indicators of women with a physiological course of pregnancy (Table 1). The analysis showed that

the course of the present pregnancy in 32 out of 53 examined pregnant women who had a history of massive bleeding proceeded without complications, and 38 pregnant women were found to be at risk of miscarriage. In this regard, we decided to divide them into 2 groups: without the threat of miscarriage and with the threat of miscarriage. An individual analysis of the indicators of endothelial dysfunction showed a pronounced dysfunctional state in pregnant women of the group at risk of miscarriage. So, if at 18-24 weeks of pregnancy in the blood serum of pregnant women without signs of miscarriage, an increase in the level of ET-1, NO, E-selectin and VEGF was detected by 1.66 ($P<0.05$); 1.2 ($P>0.05$); 1.32 ($P<0.05$) and 1.17 ($P>0.05$) times relative to the indicators of women with the physiological course of pregnancy. In pregnant women with the threat of miscarriage, this excess was 3.33 ($P<0.001$); 1.59 ($P<0.05$); 1.72 ($P<0.01$) and 1.68 ($P<0.01$) times, respectively. It should be said that in this group of pregnant women the level of ET-1, NO, E-selectin and VEGF in 2 ($P<0.001$); 1.32 ($P<0.05$); 1.31 ($P<0.05$) and 1.44 ($P>0.05$) times the values of pregnant women without the threat of miscarriage. Consequently, the indicators of endothelial dysfunction increased more markedly in pregnant women at risk of miscarriage. Analyzing the results obtained, it must be said that all the indicators studied by us play an important role in the development of endothelial dysfunction and are interrelated. Thus, in our studies, a sharp increase in vascular growth factor by 1.68 ($P<0.01$) times was shown relative to the values of the group of women with the physiological course of pregnancy. Under these conditions, fetoplacental insufficiency and hypoxia develop, contributing to the activation of vascular growth, in which the endothelium takes an active part. In a stable state, endotheliocytes do not proliferate. Under the influence of angiogenic growth factors and cytokines, endotheliocyte proliferation is activated, which ends with their differentiation and further maturation of the vessel or its remodeling, after which the newly formulated vessel becomes stable. The second molecule analyzed by us, NO - exerts a variety of homeostatic effects as an activator of soluble guanylate cyclase, one of which is involved in angiogenesis and a regulator of smooth muscle contraction and vascular endothelium, participates in angiogenesis. Its last function is associated with an increase in the permeability of the endothelium, which is necessary for the release of plasma proteins (fibrinogen), which leads to the formation of a fibrin base for subsequent migration of endotheliocytes. Apparently, this is why we observed an increase in nitric oxide by 1.59 ($P<0.01$) times in pregnant women with a risk of miscarriage who had a history of massive bleeding. It should also be said that the vasodilatory action of nitric oxide is directed against the vasoconstrictor action of endothelins. However, in our studies, the level of ET-1 increased by more than 3 ($P<0.001$) times, while the level of nitric oxide only by 1.59 ($P<0.01$) times, which is clearly insufficient to eliminate vasoconstriction. It should be said that activation of the expression of endothelial adhesion molecules, in particular E-selectin, plays a great role in the mechanism of endotheliocyte migration. E-selectin is expressed by endothelial cells and is involved in stopping neutrophils (the first stage of migration). It serves as a chemotactic signal for neutrophils and additionally activates β2-integrins, which leads to increased migration of cells containing these integrins, so we observed its increase by 1.72 ($P<0.01$) times relative to the values of the group of women with the physiological course of pregnancy.The process of angiogenesis is necessary for long-term adaptation of tissues in conditions of damage.

In subsequent periods, women with preserved pregnancy (37-39 weeks) who had a history of massive bleeding maintained high values of endothelial dysfunction. Thus, in all 20 examined women, the level of ET-1 in the blood serum increased statistically significantly by 1.32 ($P<0.05$) times relative to the values of the previous period and was significantly higher by 3.1 ($P<0.001$) times than the values of pregnant women with a physiological course. The values of nitric oxide and E-selectin remained within the values of the previous study period, exceeding the values of the control group of pregnant women by 1.54 ($P<0.05$) and 1.66 ($P<0.05$) times. At the same time, the content of VEGF, as well as the level of ET-1 increased by 1.24 ($P>0.05$) times relative to the values of the previous study period. This indicator significantly exceeded the values of the group of pregnant women with a physiological course by 1.71 ($P<0.01$) times. However, it should be said about the high individual variability of the studied indicators. In this regard, we analyzed individual indicators depending on the course of this pregnancy. Since preeclampsia was the most common concomitant obstetric pathology in this group, we divided the group into 2 subgroups: without

preeclampsia and with preeclampsia. Studies have shown that in pregnant women without signs of preeclampsia at 37-39 weeks of pregnancy, serum levels of ET-1, NO, E-selectin and VEGF increased by 2.13 (P<0.05); 1.41 (P<0.05); 1.37 (P<0.05) and 1.26 (P>0.05) times relative to indicators of women with the physiological course of pregnancy. In pregnant women with preeclampsia, this excess was 3.73 (P<0.001); 1.63 (P<0.01); 1.85 (P<0.01) and 2 (P<0.001) times, respectively. It should be said that in this group of pregnant women, the level of ET-1, NO, E-selectin and VEGF is 1.75 (P<0.001); 1.16 (P>0.05); 1.35 (P<0.05) and 1.59 (P>0.05) times the values of pregnant women without clinical manifestations of preeclampsia.

Consequently, in pregnant women who have had a history of massive bleeding, manifestations of endothelial dysfunction persist in subsequent pregnancy both in early and late pregnancy. This, in our opinion, predisposes to the risk of microcirculation disorders in the maternal side of the placenta, causing the development of miscarriage in the early stages or preeclampsia – in the later stages of gestation. In our opinion, to assess the state of the vascular endothelium, it is advisable to determine the level of ET-1 and VEGF in the dynamics of gestation. Analyzing the data obtained, we can say that the main mechanism for the development of preeclampsia is placental insufficiency due to inadequate remodeling of the maternal vascular network in the interstitial space. This stimulates the placenta to release vasosuppressors and other soluble factors into the maternal bloodstream in order to activate the maternal body to create more efficient fetal circulation. However, this leads to systemic endothelial dysfunction of the mother's body and the development of hypertension, proteinuria, the manifestation of disorders of the functions of the brain and other organs and systems in pregnant women with preeclampsia. Consequently, pre-gravidar treatment and rehabilitation of pregnant women who have had a history of massive bleeding significantly reduce the high values of the main indicators of endothelial dysfunction. This has a positive effect on the course of subsequent pregnancy, which coincides with clinical indicators.

Based on the data obtained, the following conclusions can be drawn:

1. Pregnant women who have had a history of massive bleeding develop endothelial dysfunction, manifested by a sharp increase in the serum level of endothelin-1, a moderate increase in the content of nitric oxide, E-selectin and vascular growth factor. The severity of these changes increased as the gestation period lengthened.
2. The dynamics of changes in indicators of endothelial dysfunction in pregnant women who had a history of massive bleeding in the anamnesis depended on the course of the present pregnancy, more pronounced in pregnant women with the threat of miscarriage at 18-24 weeks of pregnancy and with preeclampsia at 27-37 weeks of gestation. More indicative is the determination of endothelin-1 and vascular growth factor.
3. Carrying out therapeutic and preventive measures in pregnant women who have had a history of massive bleeding leads to a decrease in high values of endothelin-1, nitric oxide, E-selectin and vascular growth factor in blood serum, correction of the dysfunctional state of the endothelium, which leads to a decrease in complications during pregnancy and childbirth.

Literatures:

1. Ayupova F.M., Karimova N.N., Yakhyaeva F.O. "Comparative assessment of the conditions of women who have suffered massive bleeding" //Dermatovenerology and reproductive health news. - Tashkent, 2013.-No.3-V, -pp.13-16.
2. Ayeni D.O. Endothelial dysfunction in the genesis of early reproductive losses. – Abstract of dissertation...Candidate of Medical Sciences – 2012. – 22s.
3. Karimova N.N., Poyanov O.Y., Akhmedov F.K., Zokova N.R. "Some biochemical mechanisms of endothelial dysfunction in women who have suffered massive bleeding in childbirth" // Doctor akhborotnomasi. - Samarkand, 2020. – №2(94). – Pp. 47-51.
4. Kayumova G.M. Sarkisova L.V. Features of the clinical course of premature birth and perinatal outcomes //Collection of materials of the first Bukhara International Conference of

Medical Students and Youth. -2019. –pp. 262-263.

5. Karimova N.N., Akhmedov F.K., Azimov F.R., Rustamov M.U., Oripova F.Sh. "Clinical analysis of birth histories with postpartum bleeding taking into account rehabilitation measures"// Tibbietda yangi kun. – Tashkent, 2019.-№1(25). -P.99-103.6. Majerczyk M., Olszanecka-Glinianowicz M., Puzianowska-Kuźnicka M., Chudek J. Retinol-binding Protein 4 (RBP4) as the Causative Factor and Marker of Vascular Injury Related to Insulin Resistance. Postepy Hig Med Dosw (Online). 2016, Dec 21; 70(0): 1267-1275.
6. Karimova N.N.,Ayupova F.M., Rustamov M.U. “Analysis of childbirth stories with postpartum hemorrhage, taking into account rehabilitation measures and future of reproductive system after massive obstetric bleeding” International //Journal of Pharmaceutical Research, **Scopus** / Jan-Mar 2019/Vol 11. Issue 1. -P.1690-1695.