PREGNANCY AND ISSUES WITH INHERITED AND ACQUIRED THROMBOPHILIA

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SUMMARY:

Pregnancy is hypercoagulable state. The field of thrombophilia; the tendency to thrombosis, has been developed rapidly and has been linked to many aspects of pregnancy. It is recently that severe pregnancy complications such as severe preeclampsia, intrauterine growth retardation, abruptio placentae and stillbirth has been shown to be associated with thrombophilia. Recurrent miscarriage has also been associated with thrombophilia. The incidence of all types of thrombophilia (inherited and acquired) in women with obstetrical complications is not so rare and every specialist should think about these conditions and has to investigate and to suspect them in their patients with recurrent fetal loss or severe complication of the pregnancy.

Approximately 1 to 5 percent of pregnant women have serious complications of pregnancy, such as severe preeclampsia, abruptio placentae, intrauterine fetal death, or severe fetal growth retardation. The rates are even higher among older women, those with preexisting vascular disease (e.g., chronic hypertension, renal disease, or type 1 diabetes melUtus), those With multiple fetuses, and those who have a history of one or more of the complications during a previous pregnancy. These obstetrical complications are associated with intervillous or spiral-artery thrombosis and inadequate placental perfusion, and their causes will be discussed in the following review.

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The following complications in women during pregnancy could occur: implantation failure, miscarriages, preeclampsia, intrauterine growth retardation, oligohydramnios (low levels of amniotic fluid), abruptio placenta, premature labor and delivery (often caused incompetent cervix syndrome), unexplained intrauterine fetal death, thrombophlebitis (blood clots in the veins or the arteries during pregnancy)

Adverse pregnancy outcome in women with thrombiphilia are not rare, causes are unknown, but all of them may be associated with abnormal placental vasculature and disturbances of hemostasis leading to inadequate matemal-fetal circulation . Endothelial dysfunction, vasoconstriction, placental ischemia and enhanced coagulation are associated with abnormal placental development which may lead to inadequate fetomatemal circulation and decreased placental perfusion. In normal pregnancy the trophoblast invades the spiral arteries which lose their muscular wall and become flaccid allowing maximum blood flow to the placenta. The abnormal interaction between mother and fetal allograft in abnormal pregnancies leads to abnormal trophoblastic invasion of the spiral arteries, resulting in small narrowed vessels. The subsequent vasculopathy and secondary thrombosis from hypercoagulability may result in inadequate perfusion of the intervillous space, preeclampsia, placental infarcts, IUGR, placental abruption and IUFD. Placental pathologists use the term placental vasculopathy to describe pathological placental changes characterized by superficial endovascular cytotrophoblast invasion in the spiral arteries, acute atherosis and thrombotic processes in the spiral arteries and/or the intervillous space.

For diagnosis of inherited thrombophilias should be investigated some labs and genetic factors -Leiden Factor V mutation R560Q (DNA test by PCR), hyperhomocysteinemia MTHFR C677T and A1298C mutations (DNA test by PCR), prothrombin Gene Mutation 20210 (GA) DNA test by PCR, Protein C levels, Protein S levels, activated Protein C activity and PAI-1 gene mutation

About 15% of all pregnancies will terminate in miscarriage. Recurrent miscarriage (RM) is a condition defined as three consecutive miscarriages and affects 1% - 2% of women of reproductive age. Up to 5% have >. 2 recurrent losses. These sporadic miscarriages are the commonest complication of pregnancy and are mainly due to chromosomal abnormalities in the fetus. Women with thrombophilia are at increased risk for thrombosis during

pregnancy and adverse maternal and fetal sequelae. The haemostatic system plays an important role in the success of pregnancy and the process of implantation, and placentation This contact between placenta and maternal circulation is crucial for the success of pregnancy. Prothrombotic changes and thrombosis may interfere with these processes leading to miscarriage. This may explain many cases of previously unexplained RM Few studies reported on an association between IUGR and thrombophilias. Mainly severe preeclampsia is associated with FV Leiden mutation hyperhomocyteinemia, and deficiencies of protein S C and AT III. Coagulation inhibitors and abnormalities of the homocysteine metabolism as risk factors for placental vasculopathy and abruptio placentae. A recent meta-analysis regarding thrombophilic disorders and fetal loss shows that Factor V Leiden was associated with early and late recurrent fetal loss, and late non-recurrent fetal loss. Activated protein C resistance was associated with early recurrent fetal loss, and prothrombin G20210A mutation with early recurrent and late non-recurrent fetal loss. Protein S deficiency was associated with recurrent fetal loss and late non-recurrent fetal loss. Methylenetetrahydrofolate mutation, protein C, and antithrombin deficiencies were not significantly associated with fetal loss

For diagnosis of acquired thrombophilias should be investigated (Antiphospholipid syndrome in particular) antiohospholipid antibodies to six phospholipids of the IgM, IgG and IgA classes. Lupus anticoagulant antibody. Activated Partial Thromboplastin Time (APTT) and Prothrombin Time (PT), Partial Prothrombin Time (PTT). Antiphospholipid antibodies (aPL) are a family of autoantibodies with specificity for negatively charged phospholipids, or more accurately for their complex to phospholipid binding proteins. Their presence is associated with arterial/venous thrombosis and recurrent pregnancy losses. These clinical manifestations with the persistence of aPL are recognized as antiphospholipid syndrome (APS), one of the most common acquired thrombophilia. Beta 2-glycoprotein I (beta 2GPI) bears the epitope(s) for anticardiolipin antibodies (aCL) on its molecule, and lupus anticoagulant activity depends on the presence of beta 2GPI or prothrombin. Thus, phospholipid binding proteins may have some crucial roles in the pathophysiology ofthrombotic events in APS. It has been hypothesized that aPL bind to cells and induce procoagulant activity via phospholipid binding proteins. The APS is associated with placental vascular thrombosis, decidual vasculopathy, intervillous fibrin deposition, and placental infarction. These pathological changes in the placenta may result in miscarriage, IUGR, stillbirth, and early severe preeclampsia. In relation to fetal loss, positive test for aCL or presence of LAC may be found in up to 20% of women with recurrent pregnancy loss. It may present with either recurrent embryonic loss, or fetal demise beyond 10 weeks of gestation and is found in 10-15% of women with fetal death beyond 20 weeks of gestation

The incidence of all types of thrombophilia (inherited and acquired) in women with obstetrical complications is so high that every specialist should think about these conditions and has to investigate and to suspect them in their patients with recurrent fetal loss or severe complication - preeclampsia up to 68%, abruptio placentae - 70%, Intrauterine Growth Retardation - 61%, stiUbom babies- 58%.

The management of thrombophilia during pregnancy encompasses some protocols with two main goups of medicine - low molecule weight heparine and aspirin. In the management ofthrombophilias the two main branches are - prophylaxis and treatment. Primary thromboprophylaxis is in asymptomatic women, secondary prophylaxis of recurrences" in women who have previously developed thrombosis, and the treatment of acute thrombotic episodes. The protocols include 0.3 ml subcutaneous low molecule weight Heparin per day after the heart beating of the fetus has been seen with transvaginal ultasonography and low-dose aspirin starting at early first trimester (100 mg Aspirin per day)

The most studies and clinical centers recommended those patients with the following should be investigated for thrombophilia- recurrent pregnancy losses, infertility, implantation failures, IVF-ET failures, thromboembolic disease at a young age with no provoking event, a positive family history, or whose thrombosis involves an unusual site.

In conclusion could be said that thrombophilia, inherited or acquired, is very common. Any woman experiencing any of the above complications of pregnancy deserves to be tested. Any relative of any woman experiencing the above complications should demand testing before a pregnancy is planned or initiated.

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