**Update in Immune Thrombocytopenia (ITP) During Pregnancy**

Receiving a diagnosis of immune thrombocytopenia (ITP) at any time can feel overwhelming and scary. This is especially true during pregnancy when emotions are heightened and there is a constant adjustment to the physical demands of pregnancy. A new or returning diagnosis of ITP during pregnancy can add an additional layer of stress, wondering how ITP will impact overall health, pregnancy, and the health of the developing baby.

ITP is diagnosed in approximately 1 in every 1,000-10,000 pregnancies and represents 4-5% of all cases of pregnancy-related thrombocytopenia. While ITP may present at any time during a pregnancy, it is the most common diagnosis of thrombocytopenia in the first trimester. Gestational thrombocytopenia generally presents much later in pregnancy and platelet counts are usually above 70,000. ITP in pregnancy commonly presents with a platelet count below 70,000-80,000 µL. It is also more common in individuals who have had ITP previously. The diagnosis of ITP in pregnancy is made by excluding other possible underlying causes of thrombocytopenia by a detailed physical examination and medical history, taking a thorough prenatal history of both current and past pregnancies, and blood work. A slight drop in platelet count is normal in any pregnancy as blood volume expands. Platelets commonly fall 10% in the average pregnant woman and usually does not result in thrombocytopenia.

Pregnancy is not contraindicated in women with ITP. If you have ITP you do not have to avoid or terminate a pregnancy, or worry about an increased risk for miscarriage.

Approximately 1/3 of pregnant women with ITP will require treatment. There are some medications used to treat ITP that may affect a developing baby. It is important for pregnant women with ITP to discuss their current medications with a hematologist to ensure their treatment is not contraindicated for pregnancy. Management of ITP during pregnancy depends on the severity of the thrombocytopenia. Having a platelet count between 20,000-30,000 µL may be okay if there are no bleeding issues, however it is recommended to increase the platelet count to a minimum of 50,000-70,000 µL for spinal anesthesia and at least 70,000 for an epidural. Although vaginal deliveries can be safely performed at 30,000 most obstetricians prefer the platelet count to be above 50,000 in case a Caesarean section is required. Mode of delivery in women with ITP should be based purely on obstetrical indications. Vaginal delivery is safe for the baby.

In late 2019, a global group of ITP experts published the International Consensus Report on primary immune thrombocytopenia, which covered recommendations for diagnosis and managing ITP in pregnancy. Included is the necessity to examine blood work to look not only at the platelet count, but also the red and white blood cells to rule out other conditions in pregnancy that could mask true ITP. The presence of red blood cell fragmentation can be a sign of preeclampsia (also known as toxemia) that is a common hypertensive pregnancy induced condition that can lower platelet counts. Other updates included the recommendation that it is not necessary for pregnant women with ITP to undergo an invasive bone marrow biopsy unless they have atypical features of ITP. Examples of atypical ITP may include an enlarged spleen, unresponsiveness to corticosteroids, platelets atypical in size (larger or smaller than normal), or having abnormalities in their red and/or white cell counts in addition to their abnormal platelet count. Anti-platelet antibody testing is not helpful in distinguishing between autoimmune thrombocytopenia and gestational thrombocytopenia and is not indicated. Thrombopoietin (TPO) serum testing is not recommended in pregnancy either. Attempts to measure fetal platelet counts are discouraged as they carry significant risks and do not change the mode of delivery.

Treatments include typical first-line therapies such as corticosteroids and IVIG. If unresponsive, the International Consensus Report suggests combining two first-line therapies (such as IVIG and prednisone) for a synergistic affect. Rituximab may be used during pregnancy in cases where there is serious bleeding risk, however usually avoided as it will suppress the immune system of both babies and mothers for up to 9 months depending when it is given. Other drugs that can be safely used to treat ITP in pregnancy include azathioprine and cyclosporine. Reports of the use of TPO-RAs in pregnancy have not revealed any safety issues but the numbers of patients have been small. If splenectomy is required, the consensus report suggests it be performed in the second trimester, but this is very rarely necessary. Drugs to avoid include vincristine, danazol, cyclophosphamide, and mycophenolate mofetil (MMF).

**Does ITP worsen during pregnancy?**

Many women wonder if their ITP diagnosis will worsen in pregnancy. Until recently, this question had not been investigated. In other autoimmune diseases, such as lupus, pregnancy has been shown to worsen disease or spark ‘flare-ups’ in symptoms. Other autoimmune diseases, such as rheumatoid arthritis may get better. At the recent 62nd annual American Society of Hematology (ASH) meeting held December 5-8th, 2020, Dr. Stephanie Guillet presented new insights into ITP during pregnancy. In her study, “Outcome of Immune Thrombocytopenia in Pregnancy: A French Nationwide Prospective Multicenter Observational Case – Control Study” the effect of...
pregnancy on disease course was investigated using data obtained from thirty-three centers that are part of the French ITP Reference Center Network. Participants were recruited between 2015-2019. Over 130 pregnant women with ITP diagnosed before becoming pregnant (study group) were compared to a similar sized group of women with ITP who were not pregnant, but were of child-bearing age (control group) and matched for similar disease and treatment history. Worsening of ITP was significantly more common in the study group (52.7% vs 38.2%) and was seen primarily in the second and third trimesters. The frequency of severe thrombocytopenia and bleeding events were similar in both groups however the pregnant group was found to have been more aggressively treated. It isn’t clear if the intense treatment within the pregnancy group prevented their disease from becoming more severe.

What are the risks?
ITP is often unpredictable and can affect pregnant women differently. Health care providers focus on preventing serious bleeding events and delivery complications that could result from having a low platelet count. They also are watchful because maternal ITP in pregnancy comes with a 1/5 risk (or 20% chance) for thrombocytopenia in the newborn. Fortunately, only 4% of cases of NITP are severe and life-threatening.

It is important to acknowledge that thrombocytopenic infants of ITP mothers do not appear to experience bleeding events while still in utero. This can occur with a very different condition called Neonatal alloimmune thrombocytopenia, or NAIT. If newborns are born with severely low platelet counts, to a mother who does not have ITP, the International Consensus Report for ITP recommends parental testing for NAIT.

A second study presented at the ASH meeting by Dr. Guillet, called “Risk Factors of NITP in Pregnant Women Previously Diagnosed with ITP: Results from a French Nationwide Prospective Study,” looked at the incidence of thrombocytopenia in neonates of ITP mothers. Again, in this study they used data obtained from thirty-three centers that are part of the French ITP Reference Center Network. Participants were recruited between 2017-2019. The study enrolled 180 pregnant women who were diagnosed with ITP prior to becoming pregnant. The goal of the study was to identify risk factors for the development of neonatal thrombocytopenia. Treatment of the neonate and reported complications were evaluated as well. Just over one quarter (27.2%) of babies born to mothers with ITP were thrombocytopenic, and approximately 10% of these neonates had severe thrombocytopenia with a platelet count less than 30,000 µL. Severe thrombocytopenia was more common among mothers whose ITP worsened during pregnancy. Only two neonates had bleeding complications, one of which proved fatal, and both had a platelet count of less than 10,000 µL. The study revealed newborn thrombocytopenia is more common among women who have had previous infants with thrombocytopenia and with worsening ITP. The International Consensus Report for ITP also recommends following mothers with a rapidly falling platelet count more closely than those who have a stable but low platelet count.

What does post-delivery follow-up care look like for newborns?
Following delivery, a newborn platelet count is taken from the umbilical cord. If low, the newborn is monitored and treated if the platelet count is below 50,000 µL. The risk for serious bleeding complications is very low (approximately 1% overall). The risk for an intracranial bleed in a newborn with severe thrombocytopenia is 0-1.5%. The thrombocytopenia is self-limiting. If a newborn has persistently low platelet counts, beyond the first few months of life, some women are advised to stop breast feeding for a short period of time to see if the baby’s platelet count improves. It is fine to pump while the breast feeding is held and restart when the count improves. If it falls again it is possible that some of the anti-platelet antibodies are being passed to the baby through breast milk and breastfeeding should be stopped. This very rarely occurs and the vast majority of mothers with ITP can safely breast feed their baby.

Summary
Overall, women who are diagnosed with ITP while pregnant should be reassured that it is safe for them to continue with a pregnancy, there is no need to terminate due to their platelet disorder.

Management of ITP during pregnancy depends on the platelet count and symptoms. Most pregnant women with ITP will not have a baby with thrombocytopenia. Women with ITP who have had a previous baby with thrombocytopenia are more likely to have another newborn with low platelet count. Women with ITP who become pregnant should receive close monitoring to ensure their ITP is well controlled, and the appropriate delivery plans are in place. For more information on ITP in pregnancy, please visit our ITP in pregnancy section at www.pdsa.org/pregnancy.

Thank you to PDSA Medical Advisor Terry Gernsheimer, MD for her input. Dr. Gernsheimer authored the ITP in Pregnancy section of the International Consensus Report.