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### Discussing Liver Disease During Pregnancy

#### Dr. Buch:

There are two forms of liver disease in pregnancy; first, chronic liver disease that impacts pregnancy; second, liver disease as a result of pregnancy.

Welcome to *GI Insights* on ReachMD. Today we are honored to be joined by Dr. Nancy S. Reau. Dr. Reau is a Richard B. Capps Chair of hepatology, and Professor in the Department of Internal Medicine, division of digestive diseases and nutrition at Rush Medical College.

Welcome to the program, Dr. Reau.

#### Dr. Reau:

Thank you so much, Dr. Buch. I'm so excited to be here.

#### Dr. Buch:

Dr. Reau, let's jump right in, and let's talk about intrahepatic cholestasis of pregnancy. How is this diagnosed and treated?

#### Dr. Reau:

Yes. So it's important to know that intrahepatic cholestasis of pregnancy, or ICP, is the most common liver disease caused by pregnancy, so it's really important to have awareness. It tends to occur in the second and third trimesters, and it presents with itching, not with jaundice. And alkaline phosphatase is a little hard to interpret when you're pregnant because it goes up with pregnancy, so this is really something in the second and third trimesters when you have a woman that comes in and is really itchy. You're going to think, "Oh, maybe this person has ICP." And then the diagnostic test you're going to get is a nonfasting bile acid level. If they're fasting, they tend to be a little bit, falsely low, and so you want to get a nonfasting bile acid.

#### Dr. Buch:

That's great. And, how do we treat it?

#### Dr. Reau:

Well, the treatment is a little controversial. The standard of care is ursodeoxycholic acid, which is a bile acid, and you give that at weight-based doses, about 10 to 15 milligrams per kilo. The reason I say it's controversial is some people think it helps itching. The Cochrane Review said it really didn't help much at all but was probably safe. After that Cochrane Review, a subsequent, systemic meta-analysis really did suggest that the ursodeoxycholic acid seemed to decrease preterm birth in women that had bile acids between 40 and 100 but didn't really impact stillbirth, which is what we really worry about in these mother-infant pairs—is if the bile acids get to be too high, there's an association with stillbirth, and ursodeoxycholic acid did not seem to decrease that. But stillbirth tends to occur at levels greater than 100, and that's why it's really important to do those nonfasting levels so they're not falsely too low, and most OB/GYNs will work with the group to deliver the mother around 37 weeks or a little bit earlier if it looks like those bile acids are getting close to that high threshold.

#### Dr. Buch:

Great. And a follow-up question to that, what happens if ursodeoxycholic doesn't work for a patient? What are the alternative medicines that you reach for?

#### Dr. Reau:

Yeah, so there are a long litany of things that have been tried if ursodeoxycholic doesn't work, and most of them are going to need to be

a candid discussion because none of them are really going to be that useful, and some might be unsafe, and so it's really—if ursodeoxycholic doesn't work, it's a lot of symptomatic relief and considerations of timing of delivery. But there are a long list of things that have been tried, and that might be something that the gynecologist or the OB/GYN is interested in talking about. Just none of them are so stamped with success that we would advocate as they're truly second-line.

**Dr. Buch:**

Thank you. So here is an important question, what strategies can we use to guide women who have had intrahepatic cholestasis but want to get pregnant again?

**Dr. Reau:**

Yes. So unlike some of our liver injuries of pregnancy, intrahepatic cholestasis does tend to come back. And so this is going to be specific, this is going to be much more common if there's a family history of intrahepatic cholestasis, also affects estrogen-based birth control or hormonal control, so even if you're not contemplating pregnancy, you might still find that pruritus or cholestasis occurs in a person who elects for that type of hormone replacement even after pregnancy. If intrahepatic cholestasis runs in the family strongly or it occurred at a very early level or those bile acids were very high during pregnancy, this is a time when we often will discuss genetic testing because there are a long list of genetic abnormalities, many of which fall into the pathways of cholestasis, things like that are associated with PFIC and BRIC and some of these other cholestatic diseases. And these genetic tests might help to explain why this mother is a little bit prone to intrahepatic cholestasis of pregnancy, but there isn't going to be anything that actually allows us to prevent the onset of intrahepatic cholestasis. You're going to end up going right down that same algorithm of testing for bile acids if the woman becomes itchy, and then doing those weekly or recurrent assessments of bile acids to make sure they don't get to be in that window where there's going to be a higher risk for stillbirth.

**Dr. Buch:**

What percentage of women who have had intrahepatic cholestasis pregnancy tend to have it again in their next pregnancy?

**Dr. Reau:**

Yes. I think that these percentages are a little bit difficult. About 18 to 20 percent will have known genetic abnormalities when tested. And so that probably loses some people that had early or mild cholestasis that may not have been labeled, but I think that recurrence rates are probably around 45 to 50 percent, so frequent enough that you definitely need to have that conversation in a woman that wants to become pregnant again.

**Dr. Buch:**

But not so frequent that we would prophylactically give ursodeoxycholic?

**Dr. Reau:**

No. Again, things are often evidence-based, but there has been nothing to suggest that prophylactic ursodeoxycholic would prevent intrahepatic cholestasis of pregnancy.

**Dr. Buch:**

Thank you so much. Now let's switch to acute fatty liver of pregnancy. Dr. Reau, how can we differentiate this disease from hemolysis, elevated liver enzymes, and low platelet count, otherwise known as HELLP syndrome?

**Dr. Reau:**

Yes. So preeclampsia, HELLP, and acute fatty liver of pregnancy unfortunately, have a fair amount of overlap. Acute fatty liver of pregnancy is the most severe and is a true obstetrical emergency. If not delivered very, very efficiently, that mother has a high risk of going into liver failure. HELLP and intrahepatic cholestasis of pregnancy are going to have jaundice associated with them, so even though they might overlap with preeclampsia and other hypertensive complications of pregnancy, these two injuries are going to have a lot of jaundice, not cholestasis but jaundice. In HELLP, it's going to be unconjugated because this is hemolysis whereas in acute fatty liver of pregnancy, here the jaundice is going to be conjugated because this is liver failure or mitochondrial dysfunction.

And we use the Swansea criteria for acute fatty liver of pregnancy, which is a long list of things that concentrate on those mitochondrial abnormalities because that helps differentiate acute fatty liver of pregnancy from some of these other things. Unfortunately though, it's not very sensitive in early, and it's not very specific in late, which means that those criteria are helpful, but if you have a woman that you're concerned about but she doesn't meet the criteria, please don't dismiss acute fatty liver of pregnancy.

**Dr. Buch:**

Thank you. For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Reau about liver disease during pregnancy.

Dr. Reau, does chronic hepatitis C have an effect on maternal or fetal outcomes?

**Dr. Reau:**

Yes. We are having increased awareness that all of our chronic viral hepatitis, or hepatitides, so hepatitis B and C, have some impact on pregnancy, but both of them tend to be very, very well-tolerated. So if there's someone listening that is managing or has overlap with a woman who has hepatitis C and is pregnant, these pregnancies tend to go very, very smoothly. But chronic hepatitis C does have an association with intrahepatic cholestasis of pregnancy. So we talked about ICP earlier, and this is a condition that you want to check in those women.

Now, the new screening guidelines encourage your OB/GYN to test for hepatitis B and hepatitis C in each and every pregnancy, and so it would be uncommon to get acute hepatitis C in pregnancy that is then going to manifest as intrahepatic cholestasis, but because there is that overlap, you want to think of hepatitis C in any of your women with ICP. After that, there are a long list of things that have been shown to occur a little more frequently in hepatitis C. Some of that is going to also overlap with some of the risk factors that lead to hepatitis C, but preterm delivery, postpartum hemorrhage, and gestational diabetes, these things might be a little more common in some of our viral hepatitis or gestational diabetes and a little bit higher with hepatitis B and may be a little bit lower with hepatitis C. But either way, a lot of the preterm birth, preterm delivery, small for gestational age, these are going to be concentrating in these women that have viral hepatitis.

**Dr. Buch:**

Thank you. And moving on to a big one, nonalcoholic fatty liver disease. We'll ask the same question. What's the effect on maternal and fetal outcomes?

**Dr. Reau:**

Yes. So nonalcoholic fatty liver disease, or NAFLD, is now found in about 40 percent of adult Americans. And so we know that it is increasingly recognized in women of childbearing age, but still it tends to be lower. Remember that NAFLD is associated with metabolic syndrome, so hypertension, diabetes, hyperlipidemia, and obesity, and most women of childbearing age are not going to have those ailments. That tends to occur a little more in middle age. But we do see NAFLD in pregnancy, and if you have a woman that's got fatty liver disease pre-pregnancy, you want to do the best to talk to them about nutritional goals. During pregnancy, it is not a time to attempt to lose weight. You do want to make sure that you have appropriate weight gain targets for that pregnancy. We also see a very strong association with fatty liver disease in fatty liver disease in our pre-pregnant or pregnant population and gestational diabetes, and with gestational diabetes, there's going to be a higher risk of hypertensive complications, as well as, large birth weight children, preterm birth, also. And so we do see complications in both mothers and infants, but again, this tends to be pretty well-tolerated. We also know that there are genetic factors that lead to fatty liver disease, and so the infants born to these mothers are more likely to have fatty liver disease in their lifetime, and so, always a nice reminder that talking about healthy lifestyle and the importance of low-carbohydrate appropriate diets and regular exercise for these families is going to be important messaging.

**Dr. Buch:**

And before we conclude, are there any other thoughts you'd like to share with our audience today?

**Dr. Reau:**

Yes. So I think that pregnancy and liver disease are, thankfully, uncommon to overlap, but it is increasing. And when we look at the things that increase the risk of having pregnancy-related complications, a lot of these lifestyle modifications, whether it's alcohol use disorder or the metabolic complications that lead to fatty liver disease, are risk modifiable, so that if you have a woman that's contemplating pregnancy, you want to make sure you try to address these things pre-pregnancy and not during pregnancy. That's not the ideal time to make big changes outside of healthy drinking habits. And early recognition, these things are almost always low mortality and low morbidity if appropriately managed, and that really requires us to identify them at an early time point.

**Dr. Buch:**

This was an excellent discussion on liver diseases during pregnancy. I want to thank my guest, Dr. Nancy S. Reau, for sharing her insights.

Dr. Reau, thanks so very much for joining us today.

**Dr. Reau:**

Thank you so much, Dr. Buch.

**Dr. Buch:**

For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit [ReachMD.com/GIInsights](https://ReachMD.com/GIInsights) where you can Be Part of the Knowledge. Thanks for listening and looking forward to learning with you next time.

