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Unmasking Preeclampsia, the Great Masquerader

MR. NACINOVICH: I am Mario Nacinovich, and joining me today on the Clinician's Roundtable is Dr. Kara Rood. We will discuss her focus in maternal fetal medicine and focus our conversation on a complex disease in pregnancy that is difficult to diagnose, the progressive disease of preeclampsia. Dr. Kara Rood is a Board-Certified OBGYN specializing in maternal fetal medicine at The Ohio State University Wexner Medical Center in Columbus, Ohio. We will be discussing the symptoms and diagnosis of preeclampsia. Evidence tells us that preeclampsia is truly a dynamic process and difficult to diagnose. We will discuss some of Dr. Rood's recent research with her colleagues on a simple, rapid, noninvasive test for early recognition of preeclampsia. Dr. Rood, welcome to the program. It is a pleasure to be speaking to with you about such complicated topic that can produce such devastating adverse outcomes for both mother and children.

DR. ROOD: Thank you so very much for having me.

MR. NACINOVICH: What is preeclampsia and what causes this progressive disease?

DR. ROOD: Preeclampsia is a disease that occurs in pregnancy or the immediate postpartum period after preeclampsia. It is normally characterized by elevated blood pressure, protein in the urine, and symptoms of different organ systems that it affects, such as headache, changes in vision, right upper quadrant pain. It affects the liver and the kidneys. Preeclampsia, itself, is known very much in the disease of hypothesis. I would say none of us exactly know the underlying cause of preeclampsia. We do infer that it has to do with abnormal functioning of the placenta. However, the exact mechanism is not known.

MR. NACINOVICH: Who gets preeclampsia and how common is the disease?

DR. ROOD: About eight to ten percent of pregnancies are complicated by preeclampsia. It is somewhat difficult to predict who indeed is going to get it, but there are some known risk factors, such as women with a history of preeclampsia, women with a history of high blood pressure, first pregnancies, as well as ones with multiples like twins and triplet pregnancies.

MR. NACINOVICH: When does this occur during pregnancy?

DR. ROOD: The majority of the diagnoses of preeclampsia come in the third trimester of pregnancy. However, it can happen any time after 20 weeks, and some of the earlier onset preeclampsia are some of more concerning and more progressive forms of the disease.

MR. NACINOVICH: How many women would you say have signs or symptoms of preeclampsia during their pregnancy that may require medical attention?

DR. ROOD: Depending on the population that you serve, the population that I most likely look after is the high-risk population, and there about 25 to 30 percent of those women have some signs or symptoms that could be concerning for preeclampsia.

MR. NACINOVICH: I understand that there is actually two forms of preeclampsia, and there are also other forms of hypertensive disorders of pregnancy. What is the difference between preeclampsia, toxemia, PET, and PIH?

DR. ROOD: Currently the working definitions of them are the hypertensive diseases of pregnancy spectrum whereas those range from gestational hypertension, meaning just high blood pressure in pregnancy, to preeclampsia without severe features to preeclampsia with severe features and then a progressive form called HELLP disease. Pregnancy-induced hypertension and toxemia are some of the past definitions and terminology that we used.

MR. NACINOVICH: We have HELLP syndrome. As you mentioned, it is one of the most severe forms of preeclampsia. It can occur in about 5% to 12% of preeclamptic patients. Tell us a little bit more about this syndrome. Do you truly see it in 5% to 12% of your patients?

DR. ROOD: HELLP is definitely a more severe form of preeclampsia. It is characterized by elevated liver function tests as well as low platelets. Once we have identified this, delivery has to occur pretty quickly thereafter, given the high risk of rupture of the liver capsule and spontaneous bleeding secondary to low platelets.

MR. NACINOVICH: We know this is a very complicated topic and certainly, as I mentioned earlier, it can produce very devastating adverse outcomes for both mother and child. What is the impact of preeclampsia in terms of the health to the mother and the unborn child?

DR. ROOD: Preeclampsia, itself, is the number one reason of why we, as providers, initiate preterm births here in the United States of America. Therefore, it does have all of the risk associated with prematurity for the unborn child. Also it increases the risk of placental abruption, which can result in stillbirth for the child. Then for the mother and herself, not identifying preeclampsia early and it progresses to some of the worsening state can cause eclamptic seizures as well as stroke for the mother.

MR. NACINOVICH: Recent evidence strongly suggests that preeclampsia is also attached with later life cardiovascular events for these women. This is not just an issue restricted during their pregnancy or the postpartum period. This is something that could potentially come back in another form later in their life.

DR. ROOD: That is one of the new focuses on preeclampsia with emphasis on some of the primary care providers and internal medicine providers asking those questions about prior pregnancies, identifying women whose pregnancies were complicated with preeclampsia, therefore, so they can screen appropriately due to that risk of cardiovascular disease later in life.

MR. NACINOVICH: For those just joining us on the Clinician's Roundtable, this is Mario Nacinovich on ReachMD. I am with Dr. Kara Rood, a specialist in the area of maternal fetal medicine at The Ohio State University Wexner Medical Center. We spoke earlier about getting to understand a bit about the disease of preeclampsia and its impact. Now we are going to shift to how preeclampsia is actually currently diagnosed and discuss some of the recent newsworthy events with the release of data regarding a diagnostic that Dr. Rood and her colleagues have been focused on. First, help us understand how patients with preeclampsia are currently diagnosed.

DR. ROOD: Currently we do screening at routine prenatal visits where blood pressures are obtained and for a majority of the patients, we are still obtaining a urine dipstick to assess for protein in the urine. If any of these factors are identified, then we do a symptoms screen, asking about some of the common symptoms, like headache, changes in vision, right upper quadrant pain. If at this point here we have a suspicion for preeclampsia, then they would either go on serial blood pressure monitoring and collection of a larger volume of urine to assess for protein as well as a venipuncture to assess their liver functions, their kidney functions, and their platelets.

MR. NACINOVICH: Dr. Rood, can you speak to how difficult this is to diagnose at its current stage?

DR. ROOD: Giving our increasing complexity of our patients with more comorbidities, with hypertension, underlying kidney disease, the diagnosis of preeclampsia has become a bit more challenging as a lot of these other diseases can produce the exact same signs and symptoms as preeclampsia. Therefore, it makes it challenging from a physician standpoint to make sure that it is preeclampsia and a delivery is warranted rather than just a flair in their underlying disease, which can be managed by medication and to continue with the pregnancy.

MR. NACINOVICH: That is actually a great segue to my next question. I understand preeclampsia is called the disease of exceptions and the great masquerader, which are great monikers attached to this because it can look like so many other diseases, symptoms not specific, and it does not behave consistently. Sometimes it takes longer to progress. Other times it progresses to dangerous levels almost instantly. Tell us and the audience a little bit how this progresses. How does preeclampsia actually progress?

DR. ROOD: It is very difficult to predict how preeclampsia is going to progress. We do know that the earlier that the disease is present, a lot of the times that progresses a lot faster whereas people who are diagnosed later in the pregnancy, near the end of it, those ones do not seem to progress as quickly. That may be due to the fact that at that point there we recommend delivery for them.

MR. NACINOVICH: How difficult is it to rule out and address some of the various underlying conditions?

DR. ROOD: It can be very challenging. You can imagine we do not want to get it wrong because of the devastating effects of preeclampsia if we do misdiagnose it. As a provider, there are many times that we try to weigh the risk with benefits to try to get the mother and the baby to a gestational age where they will both have favorable outcomes, but it is very challenging.

MR. NACINOVICH: How important is it for yourself and for some of your colleagues to address the underlying conditions that are being presented?

DR. ROOD: I think it is very important. With the invention of the electronic medical records, we are fortunate to at least have some of the prior history of women, but it does take an investigative tact to figure out if somebody does have underlying chronic hypertension as the women do not always know themselves that they have been diagnosed with this, especially in some of the populations where routine medical care is not something that they have participated in prior to pregnancy.

MR. NACINOVICH: Before we discuss the specifics of your recent research, can you tell us about the collection of proteins that are misfolded and aggregate together in urine of women who have preeclampsia?

DR. ROOD: This is a very fascinating finding. We know that protein are in the urine of women with preeclampsia. However, we did not understand the confirmation in the misfolded part of these proteins in the urine. That is what was identified in the basic science component prior to creating this point-of-care test that women with preeclampsia, their proteins are actually misfolded in their urine in comparison to women without preeclampsia. They do not have these misfolded proteins. One of the most interesting parts about the misfolded proteins is the ability for it to attach to this Congo Red dye, which is kind of the premise of the test.

MR. NACINOVICH: What is the role of the Congo Red Dot Rapid Paper test or CRD paper test in identifying this collection of proteins.

DR. ROOD : Given the misfolded confirmation of these proteins, the Congo Red dye has the ability to attach to them, and that makes this test very specific for these misfolded proteins in the urine of women with preeclampsia. Whereas other non-misfolded proteins, the Congo Red dye would not attach to.

MR. NACINOVICH: You recently conducted a rather pragmatic study in 346 consecutive pregnant patients. What did you and your colleagues uncover in your research?

DR. ROOD: We identified that we as physicians do have a lot of uncertainty in diagnosing preeclampsia where, out of the 346 women that presented, 217 or about 63% of them were admitted to the hospital for further evaluation to determine if they did or did not have preeclampsia. When we looked at this population too, we found out that the test, which appeared to other biomarkers and was much more closely able to predict a diagnosis of preeclampsia based on providers reviewing the charts and also giving a diagnosis of preeclampsia. It actually showed a sensitivity of 80% specificity of 89% with a negative predicted value of 92%. I think the most impressive part is that it had an 87% accuracy to correctly diagnose preeclampsia.

MR. NACINOVICH: Everyone involved in these studies were blinded to the test results, the providers, the nurses, patients themselves. Each diagnosis of each of these patients was independently adjudicated. Why was this such an important aspect of this research?

DR. ROOD: It really does help minimize bias and ensure that the results are true results. If we knew the results of the test and especially for us that have worked with the test and had the confidence in the fact that we know that the test works, we may be less likely to diagnose someone with preeclampsia if we knew the test was negative. For those more challenging cases where we are on the fence, is it preeclampsia or is it another medical condition, that test may have swayed our management. While hopefully once the test is approved for use, that will help guide management. We would need to undergo the study without that bias involved to ensure the accurate results.

MR. NACINOVICH: You and your colleagues were working with a prototype of the Congo Red Dot Rapid Paper test that is currently under clinical development. Can you tell us a little bit about the trial that is currently underway?

DR. ROOD: Since the results of our study were extremely promising, and it does support the value of noninvasive point of care, Congo Red dot urine diagnostic test to establish or rule out preeclampsia in the clinical setting. Due to that, the enrollment for our large multicenter U.S. trial supported by GestVision has already actually achieved one-third of its target goal, and we are hoping that upon successful completion of this trial, the gestation plans to seek an FDA premarket clearance for the GestAssured test. While there are no current placebo barriers with the FDA, progress can obviously be affected by risks and uncertainties relating to a number of other important factors, which could include requests for more analysis or our ability to enroll patients in the study.

MR. NACINOVICH: That is a great way to round out our discussion with Dr. Rood. We have discussed her recent work in the diagnosis of preeclampsia, and we have certainly learned quite a bit about the signs and symptoms of this incredibly complex and progressive disease that is also associated with later-life cardiovascular events. We also were able to hear about her latest research and how a simple urine test could save lives of both mothers and unborn children.

I want to thank my guest, Dr. Rood, for joining me today on the Clinician's Roundtable. Dr. Rood, it was great having you on the program. Thank you for sharing not only your thoughts, but on behalf of all of us, thank you for your truly lifesaving research and for all the work you do each day in maternal fetal medicine. I certainly want to wish you and your colleagues much continued success. I know so many lives are depending on it.

DR. ROOD: Thank you so much.

MR. NACINOVICH: I am Mario Nacinovich. To access this episode of the Clinician's Roundtable and others focusing on women's health and some of the pioneering work to advance maternal fetal medicine, I invite you to visit ReachMD.com where you can be part of the knowledge. Thank you for listening.