Glycated Albumin to Predict Adverse Neonatal Outcomes among Women with Diabetes and Overweight or Obese Body Mass Index

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Guest: Dr. Jennifer Powers Carson from the School of Medicine at Washington University in St. Louis, Missouri.

Randye Kaye: Hello and welcome to this edition of *JALM* Talk from *The Journal of Applied Laboratory Medicine*, a publication of the Association for Diagnostics & Laboratory Medicine. I'm your host, Randye Kaye.

Diabetes during pregnancy, including both type 2 diabetes and gestational diabetes, is becoming more prevalent globally. Diabetes during pregnancy increases the risk of adverse neonatal outcomes such as preeclampsia, macrosomia, neonatal hypoglycemia, and respiratory distress syndrome. While strict glycemic control can reduce these complications, traditional tests such as hemoglobin A_{1c} are often unreliable during pregnancy due to changes in red blood cell turnover and anemia. Glycated albumin, a marker of short-term glucose control, has shown promise as an alternative. However, there are no widely accepted reference intervals or cutoffs in this population and more studies are needed.

The November 2024 issue of *JALM* features an article that investigates glycated albumin as a predictor of adverse neonatal outcomes among pregnant women with diabetes and elevated body mass index. The study explores the potential of glycated albumin as a risk predictor with the goal of establishing appropriate glycated albumin cutoffs to guide clinical interventions and improve maternal and neonatal outcomes.

Today, we are joined by the article's first author, Dr. Jennifer Powers Carson. Dr. Powers Carson is an associate professor in the Division of Endocrinology, Metabolism, and Lipid Research in the School of Medicine at Washington University in St. Louis, Missouri. She is board-certified in clinical chemistry by the American Board of Clinical Chemistry, and she serves as the CLIA Lab Director for the Core Laboratory for Clinical Studies at Washington University. Welcome, Dr. Powers Carson.

Jennifer Powers Carson: Thanks for having me today.

Randye Kaye: First question, what adverse neonatal outcomes should we be concerned about among women with diabetes during pregnancy?

Jennifer Powers Carson: These babies tend to be large for their gestational age and macrosomic at delivery, and what that means is that they may weigh 10 pounds or more, and these would be a more complicated delivery. Births often require cesarean section or if delivered vaginally, there can be shoulder dystocia. In addition, the neonates can experience hypoglycemia, hyperbilirubinemia, or respiratory distress syndrome, and any of these could cause them to have a stay in the NICU.

Randye Kaye: We hear a lot about monitoring glycated hemoglobin, which is more commonly known as hemoglobin A_{1c} for diabetes and glucose control, but your study focused on glycated albumin. For those not familiar, can you explain, what is glycated albumin?

Jennifer Powers Carson: Sure. Glycated albumin is considered a short-term marker of glucose control. It forms non-enzymatically in the blood from a reaction between glucose and albumin. Since the half-life of albumin is about 19 days, the glycated albumin represents the average amount of glucose in the blood over a span of about two to four weeks, and this is a shorter timeframe than hemoglobin A_{1c}.

Randye Kaye: Why are the traditional methods of monitoring disease, like hemoglobin A_{1c} or finger stick glucose measurements, not really optimal for patients who are pregnant?

Jennifer Powers Carson: We found that patients are often not compliant with the required four finger sticks per day and recording their glucose values every time. For hemoglobin A_{1c}, it is known to be falsely low during second and third trimesters, primarily due to hemodilution and altered red blood cell kinetics. In addition, women often experience iron-deficient anemia during pregnancy, and this may actually elevate hemoglobin A_{1c} values.

Randye Kaye: Thank you. So, can you summarize the design of your study, and what were the major findings?

Jennifer Powers Carson: Sure. I'll break it into two parts. For the first part, we prospectively recruited women with elevated BMI and type 2 or gestational diabetes and obtained blood samples from them during their second and third trimester visit to the physician, and then we measured glycated albumin in those samples. Next, we used ROC curve analysis to look at the

ability of glycated albumin to predict which of these women would experience an adverse neonatal outcome.

The area under the curve for second trimester was 0.948, which was excellent, and actually a lot higher than third trimester values. We established a cutoff of 12.3% to be used during second trimester, and that was giving 100% sensitivity and 73% specificity for predicting these adverse neonatal outcomes in those women. We didn't try to set a cutoff value for third trimester values since the usefulness was less clear, and the area under the curve lower.

For the second part of our study, we obtained samples from a biobank using 20 healthy pregnant women and sought to verify previously published trimester specific reference intervals for glycated albumin in pregnant women that had been established using those with healthy weight BMI. These samples did not verify those values, and many of them fell below the published reference intervals. We further looked at biobank samples using healthy weight BMI women and we found that those did verify the previously published reference intervals for second trimester. So, all of that together suggests women with obesity or overweight women will require lower reference ranges for glycated albumin than those that were previously established in healthy weight BMI pregnant women.

Randye Kaye: Why would you expect that there may be a need for different cutoffs or reference intervals for glycated albumin in patients who have elevated body mass index?

Jennifer Powers Carson: Yeah, a good question. There have been several studies that have shown negative correlations between glycated albumin and BMI. These were not done in pregnant women and there have even been reference intervals for glycated albumin published using multiple BMI categories. The reason for this is not completely understood, but people have suggested increased albumin turnover as well as increased inflammation in those with obesity.

Randye Kaye: And finally, where do we go from here? What additional or follow-up studies do you think are needed?

Jennifer Powers Carson: Well, our studies were from a pilot and feasibility study, so a small group of individuals. So, these results need to be confirmed in a larger population, and ideally all subjects would be able to provide both the second and third trimester sample. As we mentioned earlier, we do need to establish trimester specific reference intervals for glycated albumin in women with obesity in order for glycated albumin to be more widely used as a marker of glucose control during pregnancy.

And lastly, I would love to see randomized prospective studies utilizing our second trimester cutoff to stratify women who would be at high risk for an adverse neonatal event and provide them with more intensive glucose control compared to the prior standard of care. This could show whether or not this has the intended effect of decreasing adverse neonatal outcomes in these women. The more intensive glucose control could be from additional medication or might even be providing these women with continuous glucose monitoring.

Randye Kaye: That was Dr. Jennifer Powers Carson from Washington University in St. Louis, describing the *JALM* article, "Glycated Albumin to Predict Adverse Neonatal Outcomes among Women with Diabetes and Overweight or Obese Body Mass Index." Thanks for tuning in to this episode of *JALM* Talk. See you next time and don't forget to submit something for us to talk about.