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*Inverse Associations between Measures of Adiposity and Glycated Albumin in US Adults, NHANES 1999–2004.*

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**Guest:** Dr. Elizabeth Selvin is a Professor of Epidemiology at the Johns Hopkins Bloomberg School of Public Health and holds a joint appointment at the Johns Hopkins University School of Medicine.

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

While glycated hemoglobin, known as hemoglobin A<sub>1c</sub>, is the standard metric for glycemic control in patients with diabetes, there are other glycemic markers that may overcome some of hemoglobin A<sub>1c</sub>'s limitations. Glycated albumin is a shorter-term marker of glycemic control that was cleared by the US FDA for the management of diabetes in 2017. However, unlike hemoglobin A<sub>1c</sub>, diagnostic thresholds for glycated albumin have not been established. Further, while adiposity is generally associated with insulin resistance, hyperglycemia, and elevated hemoglobin A<sub>1c</sub>, some studies have suggested a perplexing inverse association between glycated albumin and adiposity measures.

The July 2023 issue of *JALM* features a study that investigated the associations between glycated albumin and several measures of adiposity, including the National Health and Nutrition Examination Survey database of US adults. The authors also compared the sensitivity and specificity of glycated albumin for detecting hyperglycemia in adults with and without obesity. Today, we're joined by the senior author of the article, Dr. Elizabeth Selvin. Dr. Selvin is a professor of epidemiology at the Johns Hopkins Bloomberg School of Public Health and holds a joint appointment at the Johns Hopkins University School of Medicine. Dr. Selvin has devoted her career to leading translational research projects designed to evaluate and improve diabetes screening, diagnosis, and patient care. Welcome, Dr. Selvin. Firstly, what led you to undertake this study to compare adiposity measures to glycated albumin?

Elizabeth Selvin: Yeah. So, glycated albumin was cleared by the FDA in 2017 for clinical use in diabetes care. So, there's really been growing interest in the use of glycated albumin as a laboratory test, and it can overcome some limitations of hemoglobin A<sub>1c</sub>. And that's why people have been kind of

interested in this measure of glycemia. And, as you know, hemoglobin A<sub>1c</sub> is our standard measure that we use to assess glucose control in people with diabetes. However, hemoglobin A<sub>1c</sub> has some limitations, and glycated albumin can overcome some of these limitations. And so, there's really a question of whether there should be a greater role for glycated albumin in diabetes care.

Randye Kaye: Well, thank you. So, what are the limitations of hemoglobin A<sub>1c</sub>, and how does glycated albumin overcome them?

Elizabeth Selvin: So, hemoglobin A<sub>1c</sub> reflects the glycation of hemoglobin in our red blood cells, which means that anything that affects red blood cell turnover or hemoglobin can affect hemoglobin A<sub>1c</sub>. So the use and interpretation of hemoglobin A<sub>1c</sub> may be problematic in patients with anemias, who have had recent blood loss, or who have hemoglobin variants. Glycated albumin is formed by the non-enzymatic glycation of albumin in serum, so it is not affected by the same factors that affect hemoglobin A<sub>1c</sub>.

Randye Kaye: All right, thank you. So why were you focused on adiposity in this study? And in what ways did you assess it?

Elizabeth Selvin: Yes. So, this has been a really interesting thing in this literature. So, I've been studying glycated albumin for a number of years now, and we've seen evidence that glycated albumin may not perform well as a biomarker of hyperglycemia in people who are overweight or obese. And because most patients with type 2 diabetes are overweight or obese, this may pose a particular issue for the use of glycated albumin as a laboratory test.

Randye Kaye: So that's a major finding, I would guess. What are the other major findings from your study?

Elizabeth Selvin: So, we measure glycated albumin in over 10,000 people who participated in the National Health and Nutrition Examination Survey, or NHANES study. And this is a national study of the US population. It's really one of the most important sources of data on the health of Americans. And we looked carefully at the associations of glycated albumin with different measures of adiposity in American adults. And what we found was that glycated albumin was inversely associated with each different measure of adiposity. So, inversely associated with BMI, with waist circumference, with fat mass, with trunk fat, and with total body fat. So, this was in contrast to hemoglobin A<sub>1c</sub>, which was positively associated with greater fat mass, with greater adiposity. So, in other words, people who had high levels of adiposity, or who were overweight, or who had obesity, had higher levels of hemoglobin A<sub>1c</sub>, but they had lower than expected levels of glycated albumin.

- Randye Kaye: Ah. Those are surprising results. So, why do you think adiposity would affect levels of glycated albumin, and why would there be that inverse relationship?
- Elizabeth Selvin: So, the short answer is I don't know.
- Randye Kaye: Okay.
- Elizabeth Selvin: Our findings are very consistent with other studies in different populations. So, it's clear that adiposity has a major effect on glycated albumin. One of the prevailing hypotheses is that maybe inflammation is at the root of all this, that proinflammatory activity of adipose tissue might increase albumin turnover. But we looked carefully at a bunch of different measures of inflammation, and that didn't seem to explain any of the observed association. So, maybe glycation of albumin is impaired by obesity-related changes in the local molecular environment that's surrounding albumin. Honestly, I don't know why we see this, but I can tell you that adiposity is definitely important in the interpretation of glycated albumin.
- Randye Kaye: All right, thank you. And the answer I don't know is what leads to more research, right?
- Elizabeth Selvin: Yes, indeed.
- Randye Kaye: So, finally, what do your results mean for the clinical laboratory and for the use of glycated albumin as a biomarker in diabetes care?
- Elizabeth Selvin: So, those are the key questions and really the important ones. So, we found that glycated albumin was very specific, but maybe not as particularly as sensitive as we would like to detect mild hyperglycemia, and the effects of adiposity may be the reason why. So this means that glycated albumin is likely very useful for monitoring glycemic control in diabetes of patients when glucose is high, when we have overt hyperglycemia, and maybe particularly useful when hemoglobin A<sub>1c</sub> testing is problematic, but it seems that glycated albumin is simply not sensitive enough to be used as a screening or diagnostic test, and that's probably because of this effect of adiposity.
- Randye Kaye: All right, thank you. Very interesting. Thank you so much for joining us today.
- Elizabeth Selvin: Thanks so much for having me.
- Randye Kaye: That was Dr. Elizabeth Selvin from the Johns Hopkins Bloomberg School of Public Health, describing the *JALM* article "Inverse Associations between Measures of Adiposity and Glycated Albumin in US Adults, NHANES 1999–2004."

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.