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Proteinuria in CKD Progression: Understanding Its Role and Monitoring Strategies

Announcer:

You're listening to *Clinician's Roundtable* on ReachMD, and this episode is sponsored by Travers Therapeutics. Here's your host, Dr. Gates Colbert.

Dr. Colbert:

Welcome to *Clinician's Roundtable* on ReachMD. I'm Dr. Gates Colbert, and joining me to discuss proteinuria's role in the progression of chronic kidney disease, or CKD, is Dr. Jared Hassler. Dr. Hassler is an Associate Professor of Pathology and Laboratory Medicine at the Lewis Katz School of Medicine at Temple University in Philadelphia. He is also a patient with IgA nephropathy and a kidney transplant recipient, which is pretty remarkable. Dr. Hassler, thanks for being here today.

Dr. Hassler:

Dr. Colbert, I appreciate the invitation to come and talk about something that is personal to me, and I have a lot of passion to teach about, so thank you.

Dr. Colbert:

Fantastic. So let's dive right in. Can you tell us how proteinuria serves as a predictor of CKD progression?

Dr. Hassler:

Yeah, that's a great question. So one of the things that I teach a lot, both to the med students and to the nephrology fellows and nephrologists, is about how at the microscopic level, in the glomerulus, the glomerular basement membranes, there's a couple of different layers to that. Whenever any of those layers get damaged, things will get through that barrier that shouldn't normally get through. The only thing that should get through is the plasma component that's been filtered. So once we start to see protein in the urine, we know that that barrier has been damaged.

Multiple different kidney diseases can do this. IgA nephropathy is one of them, but it's not the only one. And so once we start to see protein in the urine, we know that there is some kind of damage happening at that barrier level at least. There could be more in the glomerulus or the kidney itself, but we know at least at that level, there is damage happening. So it's a great indication that something is not normal, something's wrong, and possibly needs a biopsy or other workup to try to figure out what's going on.

Dr. Colbert:

And as a quick follow-up to that, how does proteinuria contribute to CKD progression and kidney damage?

Dr. Hassler:

So interestingly, when we talk about the kidney, especially at that microscopic level, there's a couple different components of it. There's the glomerulus, like I talked about with its barrier membranes. There's the tubules and the interstitium; I think of the interstitium as the glue that holds things together, and there's also other blood vessels that are supplying blood. Whenever there's damage in one compartment in the kidney, it will eventually lead to damage in the others. So in this situation, the protein that is getting through that barrier in the glomerulus, that basement membrane, it ends up in the tubules, and it starts to generate a cascade of different signals and inflammatory responses that will eventually start to scar down the tubules as well. This all leads to chronic damage over time. So if we can figure out what's causing that damage, what's causing that protein to be leaked, and potentially stop it or at least slow it down, that will decrease the progression of the chronic kidney disease.

Dr. Colbert:

So with that in mind, what are the pathophysiological mechanisms behind proteinuria's role in all of this?

Dr. Hassler:

Yeah, so it's a great question. As I've talked about the glomerular basement membrane, once you have protein in the urine, you know you've had damage there. So the protein that gets through where it shouldn't, it ends up in the tubules. And as it deposits in the tubules, things happen. So the tubules themselves will start to release cytokines and other inflammatory markers, which bring in inflammatory cells. This ends up damaging and scarring down the tubules in interstitium within the kidney. And basically, we call that just generally speaking, scarring down of the kidney itself.

So the more protein that is getting through that barrier, that glomerular basement membrane, and ending up in the in the tubules themselves, the more scar over time that's going to happen to the kidney and the worse the kidney is going to do. So if we can decrease the amount of protein that is ending up in those tubules, we'll decrease scar, which can't really be fixed at this time, and we'll also show that that's slowing down the disease progression itself.

Dr. Colbert:

For those just tuning in. You're listening to *Clinician's Roundtable* on ReachMD. I'm Dr. Gates Colbert, and I'm speaking with Dr. Jared Hassler about the relationship between proteinuria and chronic kidney disease progression. So, Dr. Hassler, that was a great explanation about the role of proteinuria in the pathogenesis of progression of CKD. So how can we monitor proteinuria levels in our patients?

Dr. Hassler:

So as a patient myself, one of the things that we would do frequently is I would have to be asked to collect a 24-hour urinalysis or at least a sample of my urine for the lab to go and measure the amount of protein. Now, Dr. Colbert, I don't know how many of your patients have had do this; they've probably complained because it's hard to have any sense of dignity carrying that jug around with you all day long. Nowadays, they have a lot of different methods that we use, like a spot urinalysis when you go in to give labs where your blood is drawn and you have to provide a urine sample; we're able to measure and appropriately estimate about how much you would be losing in a 24-hour period. And in a normal state, you would want to be losing less than 500 mg or 0. Anything over that is going to let us know that there's probably something wrong.

So as somebody that's had to do many, many 24-hour urinalyses, I'm so grateful now that I don't have to do that anymore. And it can still give an accurate amount of the amount of protein that I'm losing in a day, understanding that as that number keeps increasing, that's more damage to the kidney itself, specifically that glomerular basement membrane we talked about.

Dr. Colbert:

So we're monitoring your patients, you see that the levels of proteinuria are going up, what steps can we take to reduce that and slow CKD progression?

Dr. Hassler:

So when I was going through my own journey before dialysis and transplant at the time, all they could do was do blood pressure medications and even try fish oil pills. It possibly did slow the progression of the disease, but I still ended up on dialysis and needing a transplant. Most of the nephrologists will still start by trying to get the blood pressure under control. In that glomerular basement membrane in the kidney, blood is flowing through and getting filtered, so you can imagine if it's higher blood pressure coming through there, it's just going to be more damage. So that's always going to be one of the steps that help.

Now there are multiple different companies coming up with new drugs for each different type of kidney disease. Talking about IgA, there's multiple different companies now with different targets for ways to slow or even possibly stop the disease progression. I'm very happy with this. I wish it had been around when I was going through this myself. But, you know, I have children of my own that may have to go through this. I have many patients and friends I've met with this disease and other kidney diseases. And it gives me a lot of hope and excitement for the future that there's a lot more tools for nephrologists to use in helping patients with these kidney diseases and possibly preventing them from having to go on dialysis or need a transplant.

Dr. Colbert:

Yes, I agree. We have a lot more tools, as you mentioned, to treat IgA with different mechanisms of actions, and I really think we're going to have a positive impact as we go forward with these patients. And last question, Dr. Hassler. What kind of impact can the monitoring and reduction of proteinuria levels have on our patients?

Dr. Hassler:

So as I started with the first question that we talked about, that amount of protein is going to let you know how much damage is happening. So as we monitor the protein that's happening in your urine, if that level decreases or at least stays the same, you know that the disease is not progressing further. So I think that's a great sign.

And if the protein does actually start to increase, that gives your doctor, the nephrologist, an idea that they probably need to increase treatments, maybe switch to a different treatment, or increase the dose of what's happening. I think it really does help the nephrologist have an idea of how they need to continue to alter the treatment plan going forward with the patient.

So monitoring both the serum levels of creatinine that we do sometimes, but also the protein that's being lost in the urine, I think, is critical to help get an idea of whether the treatment's working, whether you need to increase dosage, or whether you need to try to add a different treatment.

Dr. Colbert:

Now given those impacts, I want to thank my guest, Dr. Jared Hassler, for joining us to talk about proteinuria's role in chronic kidney disease progression and how we can slow down the decline. Dr. Hassler, it was great having you on the program today.

Dr. Hassler:

Thank you again, Dr. Colbert. I appreciate it.

Announcer:

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