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Hypertension in Women: Cardiovascular Risk Across the Lifespan

Announcer:
You're listening to *Heart Matters* on ReachMD, and this episode is sponsored by Mineralys Therapeutics Incorporated Medical Affairs. Here's your host, Dr. Shelina Ramnarine.

Dr. Ramnarine:
Welcome to *Heart Matters* on ReachMD. I'm Dr. Shelina Ramnarine, and joining me today to explore how hypertension uniquely affects women—and what that means for clinical practice—is Dr. Payal Kohli. She's an Associate Adjunct Professor at Johns Hopkins University and Duke University, as well as the Founder and Medical Director of Cherry Creek Heart in Aurora, Colorado.

Dr. Kohli, thanks for being here.

Dr. Kohli:
Thank you so much for having me. I'm really looking forward to this conversation.

Dr. Ramnarine:
So to get us started, Dr. Kohli, what makes hypertension in women clinically distinct?

Dr. Kohli:
The way we think about hypertension in women has really been very rudimentary. We just think of it as a smaller version of what we see in men, but we don't realize that it actually has a completely distinct biology, a different life course, and a different clinical presentation, and it's actually a different disease.

The most obvious difference between men and women is the hormonal influences, and we know that estrogen has a really strong effect on vascular function and on blood pressure regulation. So in premenopausal women, estrogen, of course, can promote endothelial health. It can promote vasodilation. And then when we lose this after menopause, of course, our blood pressure can start to go up.

But you may not realize that there's actually sex-based differences in the renin-angiotensin-aldosterone system as well, in addition to the autonomic tone, and many of these physiologic responses are actually modulated by estrogen. And as we all know, blood vessels in women tend to be smaller. Women tend to have more microvascular disease rather than macrovascular disease. So these are all biological differences that can lead to a different trajectory of hypertension.

Men present with hypertension in a very linear fashion, but in women, it's a different trajectory. So for example, a woman could have gestational hypertension or preeclampsia, which are hypertensive disorders of pregnancy. That could then resolve, and then that could be a risk factor or prognostic factor for her developing hypertension again later in life. So we see more of this up-and-down pattern of hypertension in women, and this obviously correlates with a lot of our hormonal changes.

And then of course, we are all aware of the gender gap in treatment. We don't recognize hypertension in women. Even after we recognize it, we don't treat it nearly as aggressively. So we really have to do better for our women. And even in clinical trials, we underrepresent women, so we don't really understand how a lot of these sex differences can play in.

Dr. Ramnarine:
If we look closer at hormonal changes, how do they shape hypertension risk in women, particularly during their reproductive years?

Dr. Kohli:
It's such an interesting question because women have this unique reproductive life cycle. And we know that estrogen cycles during the

month, as does progesterone, when our ovaries are working and active during our reproductive years. And estrogen is really important for vasoprotection. We know that it increases nitric oxide production, which can lead to vasodilation. We know that it reduces endothelin-1, which is a vasoconstrictor. We also know that progesterone can reduce systemic vascular resistance as well. So both of those are really important when it comes to protecting those blood vessels.

Now, the hormone hypothesis really gets proven when we know that hormones play a role when it comes to pregnancy. Because if you think about pregnancy, the placenta is a highly vascular organ, and it's that first stress test that a woman's body goes through. You can see a lot of changes in blood pressure.

And so again, this comes back to the concept of how risk in women is really evolving and really dynamic rather than static, and how it behooves us as clinicians to start to think about how to evaluate that risk, keeping those hormonal fluctuations in mind as context.

Dr. Ramnarine:
For preeclampsia and gestational diabetes, when it comes to long-term cardiovascular risk, how should we be thinking about that?

Dr. Kohli:
Preeclampsia and gestational diabetes during pregnancy put a target sign on a woman. So many women think it's just a disorder of pregnancy, but it's actually a lifelong disorder, and essentially it increases your risk of going on to have chronic hypertension by two to fourfold. It increases your risk of not just hypertension, but ischemic heart disease, stroke, and heart failure, and it even tells us that you're going to have cardiovascular disease 10 to 15 years earlier. I think what we're doing wrong is that we think, “After you deliver, it's resolved."

I really think about preeclampsia and gestational hypertension as biomarkers of risk. It's the body telling me that these blood vessels are very high risk, and I really think about treating those women more aggressively with the rest of their risk factors, even if their condition resolves after they deliver.

Dr. Ramnarine:
And as women move through menopause and later into their lives, what changes do you typically see in blood pressure and overall cardiovascular risk?

Dr. Kohli:
Menopause is the biggest inflection point in any woman's life when it comes to cardiovascular risk, and the problem with menopause is, a lot of times, because there's so many different systems involved, we often lose the forest for the trees. We forget that it's not just normal aging, but it's actually another target sign.

Essentially, what happens with menopause is the ovaries turn off their function, so we lose the protective effects of estrogen, which can lead to less of that nitric oxide that I talked about. So you have less vasodilation and more endothelin, and we start to actually increase our vascular smooth muscle tone, so we get more of that vasoconstrictive response. And what's interesting is that when you lose that estrogen and you start to have menopause, you actually get stiffening of the blood vessels out of proportion with age. So this is where a lot of people make a mistake, and they think that it's just aging—women's blood vessels get stiffer as they age just like men's do. But actually, it's an accelerated aging of the endothelium and the vasculature that we see because of menopause and the lack of those hormones.

We see a disproportionate increase in systolic blood pressure. We can also see the pulse pressure in women widening, and this becomes a marker of arterial stiffness as well. We see that more women develop hypertension after menopause and of course, the hypertension comes with all the other cardiometabolic risk factors, including cardiovascular risk and including more atherosclerosis. But you start to get weight gain, insulin resistance, and dyslipidemia as well. We know that menopause upregulates PCSK9, which is directly involved in LDL receptor metabolism, so we see a lot of women’s LDL levels go up as well.

So that's why I really think of menopause as the most important vascular and metabolic transition point in a woman's life. We really do need to make sure we pay attention to when she hit menopause, because if she hit menopause early, then that accelerates the onset of that cardiovascular disease even more.

Something that we're learning more recently and that’s been emphasized in the 2026 Cardiovascular-Kidney-Metabolic Syndrome guidelines is that dysregulated aldosterone may be at the nexus of many of the diseases that we treat in our patients, especially our older patients and our post-menopausal women, including obesity, type 2 diabetes, chronic kidney disease, and atherosclerotic cardiovascular disease.

Now, the role of dysregulated aldosterone in hypertension is something that we're recently starting to appreciate. We know that for many years, patients who have resistant or uncontrolled hypertension do sometimes respond to steroidal MRAs, which we've been using in

our practice as a way to treat their resistant hypertension. We know one of the key pathophysiologic mechanisms is that the aldosterone volume is turned up. When the volume gets turned up, your blood pressure goes up, and your body's supposed to sense that higher pressure and turn that volume back down. That doesn't happen in patients with hypertension, and then that cycle just propagates itself because aldosterone causes vascular stiffness, cardiac stiffness, and LVH, and that turns that aldosterone volume up even more and really propagates it.

We also know that sex hormones can also influence aldosterone. So estrogen in particular can stimulate aldosterone production under certain conditions, but we also know estrogen protects the blood vessels, which can partially offset the bad negative effects that aldosterone has. And we also know that progesterone acts as a natural mineralocorticoid receptor antagonist as well, so it can compete with aldosterone for receptor binding, and it promotes a natriuresis, which really helps to get rid of the excess sodium that aldosterone can lead to.

So if all of those good things happen with estrogen and progesterone, we also know that following menopause, a lot of things can change. So certainly, during the transition, we can see aldosterone levels fluctuating. We can also see the sensitivity to aldosterone start to shift. So many providers now call menopause the “aldosterone shift period” for women, because we know that after menopause, women can have increased salt sensitivity. We know naturally with the estrogen going away, their vascular stiffness goes up, inflammation goes up, and they have a higher sympathetic nervous system activity. And all of this leads to essentially a state of relative aldosterone excess mixed with a higher sensitivity to aldosterone and more of a salt-sensitive hypertension phenomena.

So now you've got the perfect storm for our postmenopausal women who are already struggling with many of the cardiometabolic effects of CKM syndrome; now, with this dysregulated aldosterone, they end up having an exaggerated aldosterone physiologic state. So that aldosterone volume gets turned all the way up, and we start to see an increase not just in their hypertension; aldosterone is involved with obesity, diabetes, vascular stiffness, inflammation, atherosclerosis, and all of those other bad effects as well. So it's really important to pay attention to that aldosterone shift that occurs, and really menopause is one of those critical periods for many of our women when it comes to risk stratifying them from a CKM perspective, especially with respect to their blood pressure.

We're also thinking essentially of targeting aldosterone with a new class of inhibitors called aldosterone synthase inhibitors, which work upstream of the MR receptor. So they don't wait for the aldosterone to be made and then try to block it; they actually work on the enzyme aldosterone synthase that makes aldosterone. And so perhaps inhibiting this at the source or at least partially inhibiting the enzyme at the source could potentially be something that could help reduce some of the cascade effects that happen with dysregulated aldosterone.

Dr. Ramnarine:
For those just tuning in, this is *Heart Matters* on ReachMD. I'm Dr. Shelina Ramnarine, and I'm speaking with Dr. Payal Kohli about unique considerations for managing hypertension in women.

So with these differences in mind, let's take a look at how they translate into real-world practice. In your experience, Dr. Kohli, where are we falling short in recognizing or diagnosing hypertension in women?

Dr. Kohli:
I think there are so many places where we could do better. Now, as I talked about before, we've historically excluded women from cardiovascular clinical trials because we're worried that they get pregnant. So we don't actually understand a lot about especially premenopausal women and their cardiovascular risk. What we end up doing is we miscalibrate and underestimate cardiovascular risk in women despite the fact that obesity, diabetes, hypertension, and all of these risk factors are going up in premenopausal women in the United States.

We also, I think, tend to dismiss symptoms and findings in women more. A lot of times, there's this perception that women tend to be high-stress, to be hyper, and to come into the office all wound up, and that's the reason that their office blood pressure is higher. It's not because they could actually have early-onset hypertension, but it's because they're too stressed out, or they're too much of a caregiver, or they've got too many things going on. And this is not just clinicians putting women into this box; it's actually women themselves who tend to think it because, again, of that perception we don't think heart disease is a woman's disease. We don't understand blood pressure thresholds and variability nearly as much in women as we do in men.

And now that the new ACC/AHA blood pressure guidelines have told us that to reduce cognitive decline, it's a Class I recommendation to keep systolic blood pressure below 120 and not 130, I really do think that this needs to be applied to women as well. We now have a recipe for reducing risk of dementia or risk of cognitive decline that's directly linked to blood pressure—of course, not to mention risk of stroke, end-stage kidney disease, heart failure, PAD, CAD, and all of these other things. So I think that's where we need to think about being more aggressive with blood pressure thresholds in women as well.

And then finally, I think we don't really understand the opportunities that we have around their reproductive visits. Many premenopausal women don't even have a primary care doctor; it's their gynecologist or obstetrician who serves as a primary care doctor. And I'm lucky to be practicing in a community where a lot of my OB/GYNs will send a woman to me when she has gestational hypertension, gestational diabetes, or preeclampsia. But I think in a lot of other communities, it doesn't always get recognized as an important issue.

Dr. Ramnarine:
You already started talking about some gaps in treatment, but where have you seen treatment gaps or any signs of undertreatment?

Dr. Kohli:
I see it happen not just in primary care; I see it even happen in cardiology. And I think the first point that I made, which was just we don't recognize it—let's say we've even gone through that door and we've recognized it. We're just not as aggressive, and I think that leads to essentially a slow residual accumulation of vascular risk over time.

So for example, the studies will tell us that clinicians are more likely to use single-agent therapy in women rather than combination therapy, despite persistent elevations. And yet we know that women, especially after menopause, tend to have more salt-sensitive hypertension, which means that they can raise their blood pressure more after a sodium load because of that vascular stiffness that I talked about. So that means you need combination therapy in those women. And we know that the new ACC/AHA guidelines say that we don't want to just turn up the volume on one single medicine. Instead, we want to think about moderate doses of multiple medications to hit the multiple pathways that are involved in high blood pressure.

We do know that women tend to experience more ACE inhibitor-related cough and more diuretic-related electrolyte imbalances. They also can have more edema from calcium channel blockers, and so we tend to use smaller doses. We worry about giving them too high a dose because of their body size. We tend to use fewer medications. And like I said, because we're worried that they might get pregnant, we actually don't use medication. So sometimes we actually delay using medications in these women for that reason as well.

Measurement of blood pressure in women is a whole different beast, right. In women, because they tend to have smaller arms, the cuff size can be different because their arm circumference is different. So one of the things I see happening a lot in practice is we use the exact same cuff for every sized patient, and we can obviously over and underestimate blood pressure quite a bit. So I do think we have a lot of work, even after we recognize hypertension, to try to figure out how we can bridge that gender gap that continues to exist. And I really want us to start to think about blood pressure not just in isolation, but really with the woman's entire cardiometabolic risk.

Dr. Ramnarine:
What are a few practical steps clinicians can take to better identify and treat hypertension in their female patients?

Dr. Kohli:
The first and most important is to take a full reproductive history. And I don't care what type of physician you are, whether you're in primary care, an endocrinologist, a nephrologist, or even a neurologist, because that reproductive history is cardiovascular history. It tells you all these possible ASCVD events and outcomes that this woman could have, and it really is a warning from the blood vessels and the body. So, when did she start menopause? When did she start menarche? Whether she's had any problems with carrying pregnancies and whether she's been on birth control—all of these are important when you're really figuring out a patient's long-term cardiovascular risk. So I think that's the first step.

The second thing I would tell physicians and clinicians to do is educate your women. You're not with them every single day; you're not with them all the time. You see them as a snapshot. So when you're seeing a 40-something-year-old woman for her mammogram or a 50-year-old woman for her colonoscopy, take a minute or two to talk about long-term cardiovascular risk and put it on her radar. Make sure that she understands that she needs to watch her sodium, that menopause is going to be a big transition, and that she needs to monitor her home blood pressure. And that way, you're really empowering and educating the patient to be a partner with you in crime so that it's not all up to you to find that high blood pressure one day in the office, but you're really starting to get some ambulatory blood pressure measurements. You're really trying to see how the patient's blood pressure performs under different physiologic environments. We know that there's nocturnal changes in blood pressure that can occur. A few hours before bed, our blood pressure starts to go down, and in the morning it rises. And we know that people who have blunted nocturnal dipping of blood pressure are going to go on to have hypertension. That's one of the earliest signs sometimes.

Dr. Ramnarine:
Thank you for those insights. I'd like to thank my guest, Dr. Payal Kohli, for joining me to discuss how we can improve our approach to hypertension care in women.

Dr. Kohli, it was great having you on the program.

Dr. Kohli:
Thank you so much for having me.

Announcer:
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