

## Gout Among Women: Not Just a “Man’s Disease”

### Transcript

**Angelo Gaffo, MD (Guest):** We need to involve more women with gout in clinical trials and we need to report outcomes in women with gout.

**Meghna Rao (Host):** Welcome back to season 2 of the *Rheumatology Advisor* podcast, *Rheum Advisor on Air*. I’m Meghna Rao, the senior editor of *Rheumatology Advisor* and the host of this podcast.

In this series, we will be joined by expert clinicians and researchers to discuss emerging and compelling topics in rheumatology. These perspectives may be related to the management of rheumatic disease, guideline updates, patient care, data from conferences and scientific meetings, and much more.

We’re also excited to announce that *Rheum Advisor on Air* was shortlisted as a finalist in the Best Podcast category for the 2022 Jesse H. Neal Awards, one of the most prestigious editorial honors in journalism. We thank you for your continued support.

Let’s dive in!

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**Meghna:** Gout has often been known for its predominance among men. While it is true that the risk for gout is 3 times higher among men vs women, due to uric acid levels, postmenopausal women, especially, form a significant percentage of a population with symptoms of unaddressed gout and a disproportionate worsening in disease burden.

To get a perspective on this disease, we're speaking with Dr Angelo Gaffo, section chief of rheumatology at the Birmingham VA Medical Center and associate professor of medicine in the Division of Rheumatology at the University of Alabama at Birmingham.

Hello, Dr Gaffo; thank you for joining me today.

**Dr Gaffo:** Oh, my pleasure to be here. I thank you for the invitation.

**Meghna:** Straight off the bat, and keeping today's topic in mind, let’s start with [a] myth you want to bust about gout.

**Dr Gaffo:** Oh, the number 1 myth I want to bust about gout is that it is all about your diet and your behavior. Many of the patients [with gout] that I see and encounter in my clinics are feeling very bad that they brought this on themselves because of things they ate or things they did, and although that can be true in certain cases, and certainly, behaviors – we're going to get to the topic of alcohol and diet – can precipitate flare sometimes, the process of

getting gout is much more complex and probably not largely affected by dose behaviors, but more by an inability to get rid of excess urate deposits by the kidneys. So, it's something that is largely outside of the patient's control.

**Meghna:** Yeah, and like you mentioned, any conversation about gout is incomplete without a deep-dive into the effect of diet.

At ACR 2021, there was [a] study by Yokose et al, which described the impact of genetics and diet on the risk for incident gout among women.

Now, based on your research and clinical experience, what would you say is the effect of diet on gout among women, especially, and are some patients genetically predisposed to gout?

**Dr Gaffo:** Yes. Most patients have some degree of a genetic component to gout. It's less common that someone's gout is going to be purely genetically driven. In most patients, I think there are genetic variants, which lead to inability of the kidneys to excrete excess urate.

[Alluding] to your question about dietary implications of gout – in general, the community of gout enthusiasts that I usually collaborate with, we have a shared view that the role of diet is overemphasized. I don't want to say that there is absolutely no role for dietary advice – there is. In most of our patients, we make recommendations about the DASH dietary approach, which can certainly reduce serum urate, but we want to largely de-emphasize the shame and the guilt of dietary behaviors in gout.

In women in particular – and we're going to keep coming back to this observation, Meghna – there are very few studies of gout in women. Many studies of gout include women and there's always the same disclaimer: “only 3% of our patients were women” [or] “only 5% of our patients were women,” so we cannot make many recommendations or observations specifically about women.

When looking at dietary effects in women's gout, a study from 2017 by Dr Leslie Harold from the CORONA gout data show that the relative contribution of dietary factors, or, specifically, what we know is associated with hyperuricemia, [such as] beef [and] seafood, it's very comparable to what we see in men.

Regarding another factor that has been rising in awareness about hyperuricemia and gout is the role of sweetened soft drinks, specifically those that have high-fructose corn syrup. The relative contribution between men and women doesn't seem to be different. More than 50% of both men and women with gout tend to [regularly] consume sweetened soft drinks.

Now, when we [take] to the other contributing factor that is commonly brought up, it's alcohol intake. Here is where we see a very interesting difference that was pointed out by the [Harold et al] study, and other studies, too, actually. Women with gout tend to have a history of alcohol intake, which

is much less than the history of alcohol intake in men with gout. Personally, I found that very interesting.

We ourselves did a study, 10 years ago, about the effect of different forms of alcohol intake in hyperuricemia. It's much more pronounced for beer than, for example, for wine. Liquor was in the middle of its impact in promoting hyperuricemia, but it was statistically significant.

**Meghna:** That's actually a very interesting observation, and I know that several experts, such as yourself, share the idea about the overemphasis of diet in gout, as you also mentioned.

Based on many research studies, the risk factors for gout were identified to be diet, obesity, and other factors. But keeping diet aside for a second, what would you say are some of the other contributing factors for gout, specifically among women, and again, are there any marked sex-based differences?

**Dr Gaffo:** I think that if you look, in general, [at] the pathophysiologic pathway of gout, in most cases, the most powerful risk factor, as we all know, is the concentrations of serum urate; it is the development of hyperuricemia, and probably, significant hyperuricemia over prolonged periods, which eventually ends up [as] the main cause of the factor for gout.

[One of the] factors associated with the development of hyperuricemia is certainly genetic variants, which multiple of them put together can lead to a state of underexcretion of urate in the kidneys, and eventually, the development of hyperuricemia and gout.

So, when these factors have been analyzed specifically in women, the role of these genetic factors in women seem to be less consistent, let's call it, than what has been found to be the case in men. So, at this moment, we cannot say that these particular genetic predisposing factors [are] affecting women.

Maybe when, in the future, we are able to recruit larger amounts of women with gout, and test them, and test their families, and things like that, then we will have a better answer from the point-of-view of genetics.

Other factors, and here, this is probably one of the most powerful factors for women with gout, is the role of medical comorbidities. This is probably a topic that I would like to emphasize that women with gout are a very distinct subgroup; it's usually the very sick people. The most common case of a woman with gout is someone who is affected by a number of medical [conditions], most likely, high blood pressure, diabetes, quite commonly chronic kidney disease, and quite commonly [among those who are considered] obese or overweight.

I quote, again, the study from Dr Leslie Harold, and more recently, a study from a group in Maastricht University in The Netherlands, which have compared the average body mass indexes [(BMIs)] of men and women with

gout, and certainly, women with gout seem to have an average larger BMI than men with gout.

**Meghna:** Dr Gaffo, just something I'm personally curious about, based on my research and what I was reading, how I've interpreted the situation is that gout among women is, obviously, not as prevalent as it is among men, but it is fairly prevalent, and has been misdiagnosed or maybe underdiagnosed due to a lack of provider and patient knowledge about the condition and its historic association with "maleness," as we spoke about. Would this be a correct interpretation?

**Dr Gaffo:** I think you're right in that it is commonly missed. Many doctors or health care professionals who are unfamiliar with the concept of gout in women may not even be aware that this is a problem that certainly can happen. I think that gout in women is less common, but the recognition, especially among older adults...because the epidemiology of gout in women is certainly very uncommon in premenopausal women. When we see it in premenopausal women, [i]n those cases, it could be driven by a particular genetic variant.

But as women move beyond the age of menopause, ie, when we see this uricosuric effect of estrogen, kind of, fading away, then their same levels of urate start catching up with those of men, and certainly, the frequency of gout rises. It doesn't rise to the level that we see in men, but it gets closer, to the point that 1 [in] 4 people with gout that you see beyond the age of 65 [years] probably will be a woman.

So yes, if you are [part of] a clinic that sees older adults, you need to be aware that gout can happen and it could be missed if someone is probably not expecting a woman presenting with gout.

**Meghna:** Right, that can, sort of, pose a problem, right? So, how can these gaps be addressed to inform better decisions about prevention, diagnosis, and treatment? Specifically, how are women approaching menopause or who are postmenopausal counseled in practices regarding their risks for gout?

**Dr Gaffo:** If I were a primary care provider dealing with a variety of populations, including middle-aged women who are approaching menopause, being aware if there is a family history of gout; that patient could have inherited a predisposition to having some genetic variants that will translate into hyperuricemia and later gout. [It] could be helpful in counseling them and all that.

Women who are approaching menopause and who are starting to accrue comorbidities, I will probably start paying attention to the risk [for] gout. Uric acid [and] serum urate is not part of the comprehension metabolic profiles that are checked usually in primary care clinics; they stopped being part of those profiles [d]ecades ago and that probably has made [it] more problematic to be aware that someone has a risk [for] gout.

If someone has a family history of gout, and these are truly medical comorbidities, I would probably check uric acid. It may be a good gauge to see if that patient is developing a risk of developing gout. Those are probably some steps in that direction.

In general, Meghna, gout is very poorly cared for in primary care communities, and just understanding, in general, [among] men and women, how gout presents and what the risk factors [are] might be quite helpful. We're all very familiar with the classic presentations, usually as episodes of intense pain, swelling, and redness, and warmth in lower extremity joints, which can become more and more persistent and nonresolving without critical flares later and development of tophi.

[Efforts that] we, rheumatologists, can [take is] to educate our wonderful primary care providers would be probably contributing a lot to identify better both men and women with gout quite early.

**Meghna:** I think you bring up some extremely important points, Dr Gaffo, especially about how sex can play such an important role in caring for these patients and [it] has to be taken into consideration.

But the one thing I wanted to talk about, before we close this conversation, [is] about gout guidelines that were developed in 2020, right? So, do you think, or will there or should there be an addendum with respect to the influence of reproductive factors on gout, and how can this can be addressed with patients and treatment provided accordingly?

**Dr Gaffo:** You know, I'm going to have a very hard time answering your question! Guidelines are tools – and I've been part of some groups developing guidelines in gout and [rheumatoid arthritis] (RA) – and when you develop these documents, you try [to make them] applicable to large [p]opulations, and sometimes, [narrowing it down] to groups that are a small minority could be hard, could make the document too dense or too long.

So, when you go into reproductive guidelines in gout, then you have to think, do we see enough, say, pregnant or breastfeeding women with gout, so we have to develop specific guidelines for that? I have a hard time thinking that we have enough patients to make a specific recommendation with that group. On the other hand, if recommendations [are developed], they will need to be just based on expert opinion because, as you probably can imagine, there are no real studies of large [numbers] of patients in this age group.

There are some things that we know about the medications that we use to treat gout and their potential effects on pregnancy and lactation. For the most part, the medications are not recommended in those age groups. Colchicine we avoid during pregnancy because it's potentially teratogenic; it can be secreted into breast milk. Allopurinol is a potential teratogen, too, so it's also not recommended during pregnancy. [Nonsteroidal anti-inflammatory drugs] (NSAIDs) can be used for treatment of flares in the first

2 trimesters, but not in the third trimester. [W]e know nothing about febuxostat and about *[inaudible]* in these age groups, so I don't think we have enough patients or enough data to make specific recommendations in the guidelines [among] these age groups.

**Meghna:** Dr Gaffo, these are definitely some wonderful insights from you, especially in light of the fact that this is Arthritis Awareness Month, and I believe Gout Awareness Day is coming up soon as well.

I hope providers can recognize and address these issues as they come up, with more research coming out in this area, but I thank you for taking the time to speak with me today.

**Dr Gaffo:** You're welcome; thanks for inviting me.

We need to involve more women with gout in clinical trials and we need to report outcomes in women with gout, specifically because we're sorely lacking data. We need to understand better the impact of comorbidities in gout in women.

I really, really thank you again for this opportunity to share these concepts with your audience.

**Meghna:** Absolutely, thank you.

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**Meghna:** Please stay tuned for more episodes in this series. For more information on *Rheumatology Advisor* and this podcast, you can reach out to us at [editor@rheumatologyadvisor.com](mailto:editor@rheumatologyadvisor.com).

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