

# Raising the Volume on Alport Syndrome: A Patient Perspective

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*Trust me, you have nothing to worry about.*

Eight redundant words repeated on four occasions. Each time, isolated hematuria would be found on routine examination. This would then be assessed through varying degrees of workup before ultimately resulting in the same arbitrary benign diagnosis wrapped in those same eight words.

I think that one of the biggest barriers to the diagnosis of rare inherited diseases is the assumption that clinical diagnosis will not change the course of care. I understand that concern: why make a diagnosis if nothing will be done with the information other than instilling anxiety in the family? Having been a patient on the other side of this diagnosis, I would make the argument that this overly paternalistic mindset begins to threaten patient autonomy.

Early diagnosis of Alport syndrome altered the course of disease for my family, allotting us an opportunity to delay progression to ESKD. The road to obtaining our diagnosis took our parents nearly 14 years; if not for our hospital's participation in research taking place in Germany, who knows how long this may have taken? Nevertheless, after they had the diagnosis, the game changed. Equipped with this information, our parents knew what they were up against and would stop at nothing to find treatment.

*I spent my days searching the internet and sending emails to every nephrologist across the US and Germany, explaining that I was a mother of four kids newly diagnosed with Alport syndrome. I was desperately searching for a treatment plan.*

The relentless effort on their behalf accompanied by the decision of one physician to respond to a mother's desperate plea is what allowed the boys to initiate treatment of a promising protocol being tested in animal models of the disease. This protocol would eventually be shown to substantially delay progression to ESKD (1).

Alport syndrome is an X-linked (85%) disease, exhibiting a wide range of genotype-based variability. These characteristics have historically created obstacles to timely diagnosis. In recent years, advances have allowed better navigation of such obstacles. However, success of current management recommendations is

greatly influenced by the age at treatment initiation, which is reliant on the age at diagnosis. When physicians are armed with incomplete and poorly powered clinical data, implementation of earlier diagnostic methods can be a challenge (1). Yet, in instances where genetic testing can be used clinically to significantly improve both diagnostic and prognostic practice, why does hesitation prevail (2)?

*A lot of people are living oblivious to the fact that they have a genetic kidney disease, and a lot will find out too late. I am lucky because I didn't have to find out about Alport in a hospital prior to getting hooked up to a dialysis machine or as I was added to a transplant waiting list. —Firstborn child describing the impact that Alport syndrome has had on him*

A similar gratitude is echoed among each of my siblings. One insightful perspective came from my youngest brother on the implications of receiving his diagnosis at the youngest age.

*I still feel that I don't have the best understanding about Alport. I know it will somewhere down the road lead to kidney failure. That makes me sick to my stomach to think about. I understand enalapril is what pushes that deadline farther and farther back, but how much more time exactly will we be given, and what kind of difference will exist between my brothers and me?*

His statement illuminates the level of uncertainty looming over him and his control over what the future holds. This is not an isolated feature among patients with Alport syndrome, yet this ambiguity is further complicated by an aspect of this disease less often considered in the management of their renal care.

Hearing loss is a large contributor to the day-to-day frustrations experienced by patients with Alport syndrome. At surface levels, this might be an aspect of the disease playing only a small role in management of their kidney function. Then again, even the best patients will fail to follow management recommendations that they never hear.

Preparing questions to ask about the stage or prognosis of one's disease can be intimidating on its own. Imagine the frustrations that must arise as a young, hard-of-hearing patient.

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*I'd be asked the same couple of questions, like have you been taking your medicine, or has your urine been significantly dark lately? Then I'd be sent on my way. Most of the appointment was spent asking what had been said or if the doctor could repeat themselves, because I wasn't able to understand them as they asked questions while facing their computer.*

It is easy to see how a physician could forget to consider how high they hold their papers or what seating position would maximize time spent facing the patient. The importance of increasing the sensitivity to this aspect of patient care is highlighted by unfulfilled laboratory tests, missed medication adjustments, and inconsistencies existing between recommended visit frequencies and actual visits. It would be naïve to discount external factors contributing to the adherence of this age group; however, discussion of these discrepancies reveals a common unawareness that adjustments had ever been made. Even with top of the line hearing aids and wonderful physicians, information crucial to the management of their health can be missed.

Awareness of the adversities faced by my brothers instilled a unique intricacy to the frustration that I felt growing up as a girl with X-linked Alport Syndrome (XLAS). Early on, I was told that I was a carrier of Alport syndrome; therefore, I would not experience the symptoms afflicting my brothers, and I would not be eligible to donate my own kidney as the need arose. Such a lapse in control in this manner is a frustration very difficult to explain.

Over the years, the evolution of Alport research has come to highlight the inaccuracies of a benign "carrier" as it pertains to women with XLAS (3). This deviation in semantics removed the security blanket that had provided relief to many women patients. Although statements referring to women with XLAS as carriers are not wrong, allowing the definition to end at that creates an opportunity for preventable consequences to manifest.

*"For much of the 20th century, affected females in families with AS were assumed to follow a benign course. Alport himself*

*wrote in 1927 that "females have deafness and hematuria and live to old age." Interestingly, the family first reported by Alport included a female with hematuria and deafness who died at 24 years of age" (3).*

This excerpt comes from a natural history paper published by Michelle Rheault (3) that goes further to highlight the risk of ESKD in women patients as interpreted by the data of a European study on XLAS female heterozygotes. Information in this article demonstrated presence of microscopic hematuria in 95.5% and development of proteinuria in 75% of the 365 patients in the study. Ultimately, 12% of these patients progressed to ESKD by age 40 years old, and 30%–40% progressed to ESKD by age 60 years old (3).

It has been 17 years since these data demonstrated the risk of ESKD in women patients. The evidence that these patients should not be ignored is there, yet these patients are still being told those familiar eight words.

*Trust me, you have nothing to worry about.*

#### **Author Contributions**

M. Dunleavy wrote the original draft, and reviewed and edited the manuscript.

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