Gaining a Deeper Understanding of Rare Kidney Diseases: Insights from RaDaR

By Muhammad A. Mujtaba and Divya Monga

The definition of rare kidney disease (RKD) differs globally. In Europe, a disease is defined as rare when the prevalence is <1 in 2000 individuals, whereas in the United States, the designation of rare disorder applies when <200,000 Americans are affected (1).

Recent findings published in *The Lancet*, "Effects of Rare Kidney Diseases on Kidney Failure: A Longitudinal Analysis of the UK National Registry of Rare Kidney Diseases (RaDaR) Cohort" (2), offer insights into the unique challenges and outcomes faced by individuals with an RKD. This retrospective study used extensive data from RaDaR, including individuals from across 108 UK kidney care facilities, tracked over a median of 9.6 years. The stark contrast in outcomes between these patients and the general population with chronic kidney disease (CKD) calls for a re-evaluation of our current medical and research strategies.

Data were collected for 27,285 patients in 28 rare disease groups. The primary outcomes included mortality and kidney failure. Analyses indicate that people with RKDs face a disproportionate risk of kidney failure, with a significantly higher 5-year cumulative incidence (28%) compared with the broader population affected by all causes of CKD (1%). Notably, despite the greater risk of kidney failure, these patients show better survival rates when compared with the population with all-cause CKD, reflected in a standardized mortality ratio of 0.42.

This paradox highlights a crucial aspect of RKDs: their complex, aggressive progression to kidney failure, which necessitates more intensive and prolonged use of kidney replacement therapy (KRT). The variation in outcomes, such as age at kidney failure and survival postdialysis initiation, across different RKDs underscores the heterogeneity of these diseases and the need for personalized treatment approaches (Table). Their results also align with prior data, showing that a majority of pediatric patients undergoing KRT are diagnosed with an RKD (3).

This study, therefore, provides useful insights into the prospective research domains in the field of RKDs.

1. It highlights the need for dedicated research into the pathophysiology, detection, and progression of RKDs to develop more effective management regimens. This is crucial, not just for improving patient outcomes but also for reducing the long-term demand for KRT resources. As an example, in 2023, the National Center for Advancing Translational Sciences (NCATS) funded RKD researchers, providing data to compile the Kidney Tissue Atlas (4), which is the most comprehensive human kidney cell and tissue catalog, to date. The data were gathered over more than 1 decade through the Nephrotic Syndrome Study Network (NEPTUNE), which is part of the NCATS-led Rare Diseases Clinical Research Network.
2. The establishment of centers that focus on RKDs could provide the concentrated expertise necessary for managing these complex conditions. The centers could also serve as hubs for ongoing research and clinical trials, accelerating the development of innovative therapies.
3. Increasing awareness about RKDs among health care practitioners and the public is essential. Enhanced practitioner education through dedicated seminars, webinars, and inclusion in nephrology fellowship core curriculum should be introduced. Nephrology professional societies, like ASN, the International Society of Nephrology, and the National Kidney Foundation, should also serve as training resources.
4. Enhanced support for patients is vital. This includes medical and psychological support and help in accessing the benefits of new research findings and therapies as they become available. Kidney support networks with focus on RKDs should be encouraged, similar to the NCATS-led Genetic and Rare Diseases Information Center. Genetic counselors and experts in RKDs can provide guidance to individuals and their families.

In 2017, the Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference brought together a panel of multidisciplinary clinical practitioners and patient advocates to address central issues for patients with RKDs (1). It was concluded that advancements in diagnosing and treating RKDs rely on the cooperative efforts of clinicians, patients, industry stakeholders, regulatory bodies, and government agencies.

In conclusion, the RaDaR cohort study sheds light on the significant impact of RKDs on individuals and health care systems and emphasizes the urgent need for targeted research and specialized care. By addressing these needs, we can hope to improve the quality of life and outcomes for this vulnerable group of patients, ultimately reducing the burden on health care resources dedicated to KRT.

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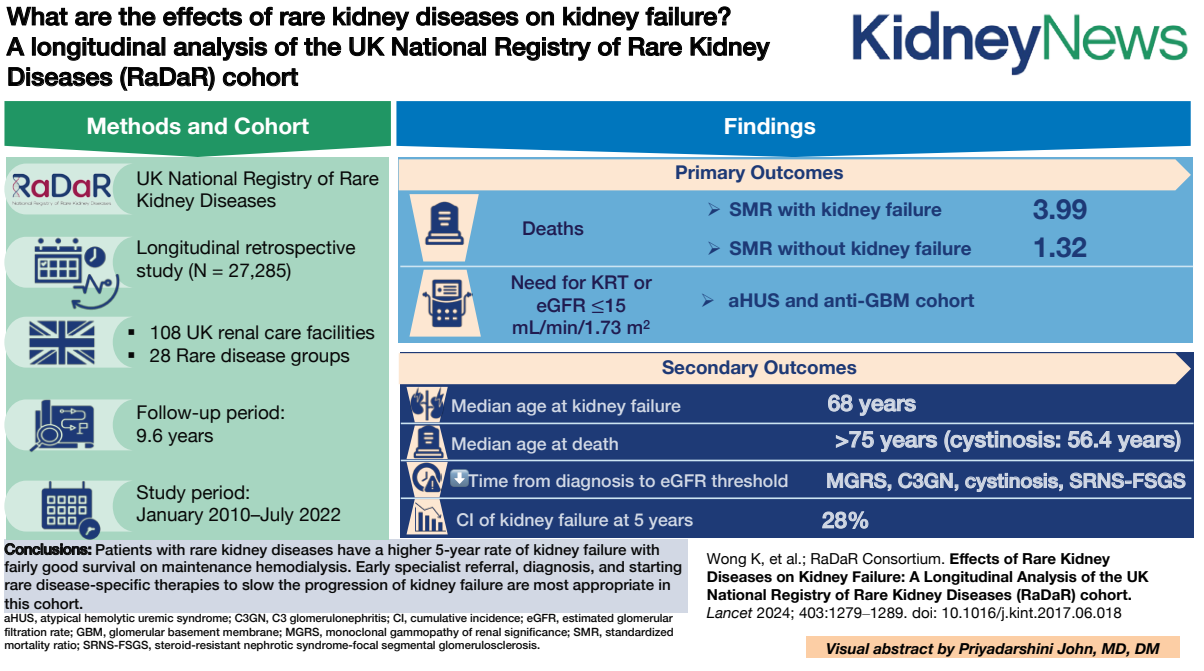
Table. Pertinent outcomes in patients with RKDs

Types of RKDs	Median age at kidney failure, years[a]	Median duration in therapeutic trial window, years[b]
Autosomal-dominant polycystic kidney disease	59	11
Cystinosis	15	8.2
Immunoglobulin A nephropathy	55	4
Atypical hemolytic uremic syndrome	41	1.8
Antineutrophil cytoplasmic antibody-associated vasculitis	89	10.5

[a]Kidney failure is defined as the need for chronic KRT or an estimated glomerular filtration rate (eGFR) of <15 mL/min/1.73 m² for 4 weeks or more.

[b]Duration in the therapeutic trial window is defined as the time between the last eGFR (≥75 mL/min/1.73 m²) and the first eGFR (<30 mL/min/1.73 m²) with no subsequent higher eGFR values.



References

1. Aymé S, et al.; Conference Participants. Common elements in rare kidney diseases: Conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney Int* 2017; 92:796–808. doi: 10.1016/j.kint.2017.06.018
2. Wong K, et al; RaDaR Consortium. Effects of rare kidney diseases on kidney failure: A longitudinal analysis of the UK National Registry of Rare Kidney Diseases (RaDaR) cohort. *Lancet* 2024; 403:1279–1289. doi: 10.1016/S0140-6736(23)02843-X
3. Wühl E, et al. Renal replacement therapy for rare diseases affecting the kidney: An analysis of the ERA-EDTA Registry. *Nephrol Dial Transplant* 2014; 29(Suppl 4):iv1–iv8. doi: 10.1093/ndt/gfu030
4. Lake BB, et al.; KPMP Consortium. An atlas of healthy and injured cell states and niches in the human kidney. *Nature* 2023; 619:585–594. doi: 10.1038/s41586-023-05769-3