



Visualizing the impact of inherited kidney disease on the burden of kidney replacement therapy

By Alberto Ortiz, Chair of ERA Registry



A major biomedical advance of the twenty-first century is the ability to cost-effectively sequence the genome, allowing a more precise genetic diagnosis. Genetic studies have uncovered a previously unsuspected phenotypic variability of inherited kidney disease (IKD) as well as misdiagnosis of the cause of chronic kidney disease (CKD) in the absence of genetic studies.

The broad categories of CKD causes represented in summary reports of major kidney replacement therapy (KRT) registries do not include IKD. This contributes to low awareness among physicians regarding the IKD contribution to the burden of KRT. This low awareness, in turn, may contribute to low prescription of genetic studies to diagnose the cause of CKD. In the absence of genetic studies, IKD may be misdiagnosed. Overall, a vicious circle is created that contributes to the underdiagnosis of IKD or their misdiagnosis as hypertensive nephropathy (as is the case for CKD caused by high risk *APOL1* variants), immune glomerulonephritis, pyelonephritis, and others. In the absence of an etiological diagnosis, there will not be an etiological treatment, a field which is rapidly advancing. For example, a phase 2 clinical trial of an intervention targeting the *APOL1* channel function was promising for proteinuric kidney disease in persons with *APOL1* risk variants¹.

Currently, the only IKD among the causes of CKD in major KRT registries is polycystic kidney disease, which is diagnosed by sonography. We now propose to add an IKD-congenital anomalies of the kidney and urinary tract (CAKUT) category to the major causes of CKD in KRT registries. The rationale is that it will contribute to visualize conditions in which genetic tests may be informative. In this regard, some forms of CAKUT are caused by genetic defects. In 2019, IKD and CAKUT were the fourth most common cause of kidney failure among incident KRT patients in the ERA Registry, accounting for 8.9% of cases (IKD 7.4%, CAKUT 1.5%) after diabetes (23.0%), hypertension (14.4%) and glomerulonephritis (10.6%). IKD and CAKUT were the most common causes of kidney failure among patients younger than 20 years (41.0% of cases), but their incidence rate was highest among those aged 45-74 years (22.5 per million age-related population). Among prevalent KRT patients, IKD and CAKUT (18.5%) and glomerulonephritis (18.7%) were the two most common causes overall, while IKD and CAKUT were the most common cause in female patients (21.6%). In conclusion, distinct categorization of IKD and CAKUT better characterizes the epidemiology of kidney disease, identifying them as the most common cause of kidney failure in females receiving KRT, and placing genetic testing as a key step in the diagnostic workup of CKD.

For more details, please attend the ERA Registry symposium on Friday, 16 Jun 2023, 08:30 – 09:45 CEST (Space 3&4)

References:

¹ Egbuna et al. Inaxaplin for proteinuric kidney disease in persons with two *APOL1* variants. *N Engl J Med* 2023; 388(11):969-979.

Incidence and outcomes of kidney replacement therapy for end-stage kidney disease due to primary glomerular disease

By Samar Abd ElHafeez, research fellow at ERA Registry



Data from renal registries showed that primary glomerular disease (PGD) is a major cause of end-stage kidney disease (ESKD) in people initiating kidney replacement therapy (KRT). Until now, most studies on the epidemiology of people receiving KRT for PGD have combined the different PGD subgroups into one “overall” PGD group¹, and only few epidemiological studies focused on different PGD subgroups².

To address this gap, we initiated a study within the ERA Registry to examine the number of patients commencing KRT with PGD as primary renal disease and their outcome after KRT using six different PGD subgroups (i.e. IgA nephropathy (IgAN), focal segmental glomerulosclerosis (FSGS), membranoproliferative glomerulonephritis, crescentic glomerulonephritis, membranous nephropathy, and other PGD). This study was performed in 69,854 individuals who started KRT due to PGD between 2000-2019 in Europe. Our findings revealed significant variations in the standardized incidence of KRT for PGD across different countries (Figure 1), with the highest incidence observed for cases with IgAN and FSGS. Interestingly, our data indicated a relatively high percentage of PGD patients categorized as “other PGD” in several Eastern European countries, such as Bosnia and Herzegovina, Serbia, Romania as well as in several Western European and Scandinavian countries such as Belgium, Spain, Norway and Sweden. This was primarily driven by the high number of cases in which histological examination of PGD was not performed, which might suggest a lack of access to kidney biopsy facilities. Consequently, the accurate reporting of true histological diagnoses could be impeded in such cases. Furthermore, our study also found variations in mortality risk among different PGD subgroups, with crescentic glomerulonephritis having the highest risk of death and IgAN the lowest. These findings emphasize the importance of considering specific PGD subgroups in understanding the burden and prognosis of individuals receiving KRT for PGD, thereby facilitating the development of personalized and equitable patient care approaches.

For more details, please attend the session “Navigating the IgA nephropathy pathway” on Saturday, 17 Jun 2023, 14:45 - 16:00 CEST

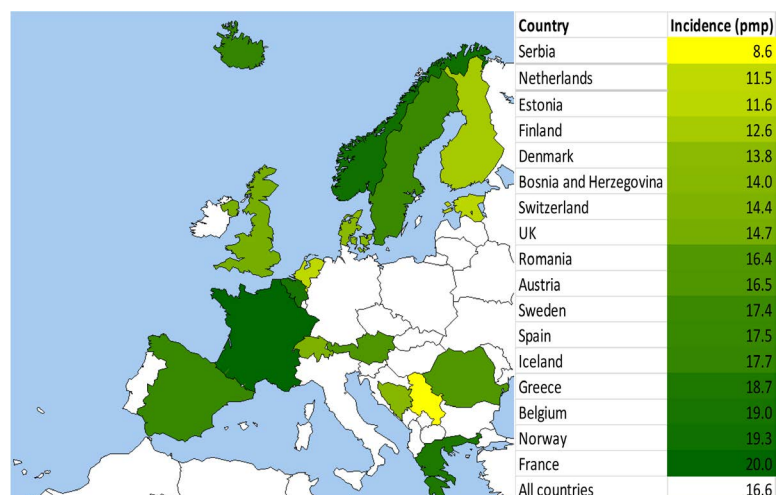
References:

¹ Stel et al. International comparison of trends in patients commencing renal replacement therapy by primary renal disease. *Nephrology* (Carlton). 2019;24(10):1064-76.

² O’Shaughnessy et al. Patient Characteristics and Outcomes by GN Subtype in ESRD. *Clin J Am Soc Nephrol*. 2015;10(7):1170.

Figure 1. Standardized incidence of kidney replacement therapy per million population (pmp) for end-stage kidney disease due to primary glomerular disease (PGD) by country based on 2000-2019 data.

For age and sex standardization, the EU28 population in 2015 was used. Dark green represents a high standardized incidence, while light green and yellow represent a lower standardized incidence.



New projects of the European CKD Burden Consortium

By Megan Astley, PhD student at ERA Registry



Studies have shown kidney function to naturally decline with increasing age, which is not currently accounted for by the KDIGO definition for chronic kidney disease (CKD) diagnosis. Because of the fixed estimated glomerular filtration rate (eGFR) threshold used in the KDIGO definition, there may be an under-diagnosis of CKD in younger people and over-diagnosis in older people. Age-adapted CKD definitions have been proposed to address this problem¹, but few studies have investigated the application of these new definitions in a large population of European adults. The European CKD Burden Consortium, which previously published a landmark paper on CKD prevalence across Europe², has planned two new projects to investigate the construction and use of age-adapted CKD definitions. For the current projects, the European CKD Burden Consortium invited general population cohorts from across Europe to participate in order to ensure a large and comprehensive population on which to carry out these studies.

The first project will describe eGFR reference values in European adult males and females who are categorized as 'healthy'. 'Healthy' individuals will be limited to those who do not have a history or presence of common cardiovascular and non-cardiovascular comorbidities, lifestyle-related risk factors, and kidney disease or dysfunction. This project will provide a comprehensive description of eGFR values in European healthy adults and a guideline for determining normal and abnormal eGFR values by age and sex.

The second project will estimate CKD prevalence across Europe using three CKD definitions: the KDIGO definition, a categorical age-adapted definition, and a continuous age-adapted definition. The categorical age-adapted definition uses three age categories with each age category having a different eGFR threshold needed to diagnose CKD. The continuous age-adapted CKD definition will use the abnormal eGFR reference values found in our first project as the threshold for CKD diagnosis in this definition.

For more information or if you are interested in joining the consortium please contact Megan Astley (m.e.astley@amsterdamumc.nl).

References:

¹ Delanaye et al. CKD: A Call for an Age-Adapted Definition. *J Am Soc Nephrol*. 2019;30(10):1785-1805.

² Brück et al. on behalf of the European CKD Burden Consortium. CKD Prevalence Varies across the European General Population. *J Am Soc Nephrol*. 2016; 27(7): 2135-2147.

ERA Registry activities during the 60th ERA Congress June 15-18, 2023, Milan

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ERA Registry Symposium

Friday, 16 Jun, 08:30 - 09:45 CEST (Space 3&4)

- Inherited kidney disease project - **Alberto Ortiz**
- Changes in epidemiology of KRT in 2020 – the first year of the COVID-19 pandemic - **Kitty Jager**
- Trajectories of end-of-life in older patients with advanced CKD - **Nicholas Chesnaye**

FC 17 Calcium Conundrums and Vitamin D Dilemmas

Friday Jun 16, 12:00-13:15 CEST (Amber 1&2)

- Association between CKD-MBD and symptom burden in older patients with advanced CKD – results from the EQUAL study - **Lorenza Magagnoli**

Kidney Transplantation

Friday, 16 Jun, 12:00 – 13:15 CEST (Focussed Oral Room 7)

- International comparison and time trends of first kidney transplant recipient characteristics across Europe: study from the ERA Registry - **Rianne Boenink**

CKD prevalence and projections - preparing for the storm?

Friday, 16 June, 14:45 - 16:00 CEST (Auditorium)

- Population ageing and how it will impact on CKD epidemics - **Kitty Jager**

Moderated orals 1.3 Kidney Transplantation (clinical and immunology)

Friday, 16 Jun, 14:45 – 16:00 CEST (Amber 6)

- Graft survival in multiple kidney transplant recipients from childhood to adulthood: an ERA Registry study from 1978 until 2019 - **Evgenia Preka**

Chronic Kidney Disease

Friday, 16 Jun, 17:00 – 18:15 CEST (Focussed Oral Room 6)

- Association between CKD-MBD and mortality in older patients with advanced CKD – results from the EQUAL study - **Lorenza Magagnoli**

Pre-emptive transplantation and which donors to choose

Saturday, 17 Jun, 12:00 - 13:15 CEST (Amber 1&2)

- Transplant survival benefit – does it apply to all patient subgroups? - **Vianda Stel**

Navigating the IgA nephropathy pathway

Saturday, 17 Jun, 14:45 - 16:00 CEST (Amber 1&2)

- Incidence and outcomes of kidney replacement therapy for end-stage kidney disease due to primary glomerulonephritis in the ERA Registry - **Samar Abd ElHafeez**