

## HIGH PREVALENCE OF RARE DISEASES IN KIDNEY TRANSPLANT RECIPIENTS IN MONTENEGRO

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Dear Editor,

According to the European registries, 24% of the pediatric and 38% of the adult patients had an unspecified or unknown primary kidney disease (1). At least some of these patients suffer from unrecognized rare disease. Rare diseases have been defined based on a prevalence of less than 5 in 10.000 people (2). Information on rare diseases and orphan drugs may be found on Orphanet which comprises >6700 rare diseases (3).

Knowledge of the primary cause of a disease is essential for adequate classification, prognosis, and most importantly, for the treatment, while it may determine the type of transplantation which in some diseases may require simultaneous multiorgan transplantation.

Montenegro is a small country in the South-Eastern Europe with population of 620.000. Country is characterized by diverse landscape with isolated communities especially in the highlands. Currently, 232 patients replace their renal function with dialysis and 127 patients have functioning renal allograft, giving the prevalence of renal replacement therapy of 217 pmp. Renal transplant program has been established in Montenegro in September 2012 in collaboration with the Croatian transplant team. Since that time, 45 transplantations were performed, two of them from deceased donors, while 82 patients who received kidneys in foreign countries have been followed at our institution.

Of adult renal transplant recipients who received renal allograft, 53 patients have unknown primary kidney disease (41.7 %). Of patients with established diagnosis, four had Alport disease, three juvenile nephronophthisis, two Dent's disease, two Balkan endemic nephropathy, while C1q nephropathy, Fanconi syndrome, De George syndrome and hemolytic-uremic syndrome were diagnosed in one patient each. Auto-

somal dominant polycystic kidney disease was cause of end-stage renal failure in 6 patients.

Of patients who are waiting for renal transplantation one patient has Jeune syndrome, one had Alport disease and one has been diagnosed with primary hyperoxaluria after ten years of hemodialysis. Six patients on the waiting list have ADPKD. Additionally, family clustering is present in four families with two to 7 involved relatives, but none of them had diagnostic evaluation.

Rare diseases (without ADPKD) contributed 11.8 % to the prevalence of RRT in our patients. However, the number of patients with rare diseases as cause of end-stage renal disease is most likely underestimated, while many of our patients had unknown primary kidney disease which at least in some of them may be an undiagnosed rare disease. Additionally, many of them have family clustering of kidney diseases. This is in line with findings of Quaglia et al. Out of 278 patients with causal nephropathy, their group found rare genetic disorders in 12 patients (4.32%) (4). If we include ADPKD which is listed in Orphanet database (3), patients with rare diseases comprise 16.5 % of our renal transplant population.

Cardinal problems in our practice are late referral to nephrologist and limited options for diagnostic evaluation. Majority of patients had no biopsy, and any specific investigation should be send abroad to European laboratories. Better education of both nephrologists and non-nephrologists to recognize the clinical features of rare kidney diseases, and timely referral of suspected patients to expert centers are essential to promote awareness of rare kidney diseases.

In conclusion, an unexpectedly high prevalence of rare genetic disorders was found in our cohort of renal transplant recipients. This number is likely underes-

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timated since many patients have unknown primary kidney disease. Earlier referral to nephrologists and comprehensive diagnostic evaluation may improve diagnosis and treatment of patients with rare diseases which affect kidneys.

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