ORIGINS OF RENAL DISEASES

Chronic kidney disease and the aging population

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Abstract

Along with instant aging of the world population the prevalence of chronic kidney disease is constantly growing. Over the past decade, the largest increase in the incidence of end-stage CKD was observed especially among subjects aged 80 and over. Realizing that renal replacement therapy is a heavy burden on health care it is critical to prevent end-stage kidney disease. To do so the risk and predisposing factors leading to development of renal failure have to be recognized. Among them are comorbidities such as diabetes, hypertension significantly associated with elderly, but also numerous of socioeconomics aspects. As the mean age of all populations is constantly increasing, reducing the risk of CKD in the elderly subjects is one of the most important challenge of modern nephrology.

Key words: renal replacement therapy, risk factors

Introduction

During 20th century the average life expectancy significantly increased, which resulted in a constantly growing number of elderly people. Already a population over 65 years old in the United States represent nearly 13% of general population. It is projected that in the next 15 years it will be a 21%.

A good source of information about the incidence and prevalence of chronic kidney disease is ERA-EDTA Registry Database [1]. Registry covers about 71% of the European population and the renal registries for most countries covering more than 98% of the population. It is estimated that one of three Europeans is at risk of developing chronic kidney disease (CKD). It is assumed that one in ten (approximately 74 million people) have already impaired renal function, unfortunately, often without being aware of it. The registry includes also incidence of patients accepted for renal replacement therapy (RRT). In total in 2013 72.698 patients started RRT. In a population of 647 million people it resulted in an overall incidence of 112 pmp (per million population) of whom 24 pmp was RRT for diabetic end stage renal disease (ESRD). The highest incidence of entering RRT among European countries was observed in Belgium, the lowest in Estonia. Overall prevalence of patients undergoing RRT is increasing. ERA-EDTA Registry shows that the prevalence of patients in renal replacement therapy in Europe increased by 2.1% from 2012 to 2013 (716.7 per million population) (Figure 1). This is also a financial challenge, given average costs up to EUR 80,000 per dialysis patient per year. Due to continuous increase in the average age of the population a further rise in ESRD patients should be expected. It complies with trend of` decreasing incidence of CKD but rising prevalence every year. Prevalence of chronic kidney disease in different countries is presented in table (Table 1).
Comparing the population of European countries to the United States of America, the incidence of patients entering the RRT during the period of 1999-2012 was three times higher in the US. The differences were particularly evident in subgroup of patients over 65 year old.

The main cause of end stage renal disease requiring starting renal replacement therapy in 2013 was diabetes mellitus, both in the population below and above the age of 65 it was around 22%. The percentage of patients with diabetic kidney disease increased from the year before. Next cause in the younger population was glomerulonephritis, while in the elderly it was arterial hypertension. Still in almost one-fifth of patients the reason of ESRD remains unknown (19.4% in the group of elderly). Way of RRT – hemodialysis or peritoneal dialysis did not change a lot throughout the years 1999-2013. A grad-

Table 1. Comparison of chronic kidney disease occurrence in different countries

Country	Study	CKD (%)
USA	NHANES III [13]	11
	Coresh J 2007[14]	13
Australia	AUSDIAB [15]	11
Japan	OKINAVA [16]	13.7
Netherlands	PREVEND [17]	7
Poland	POLNEF [7]	11.9

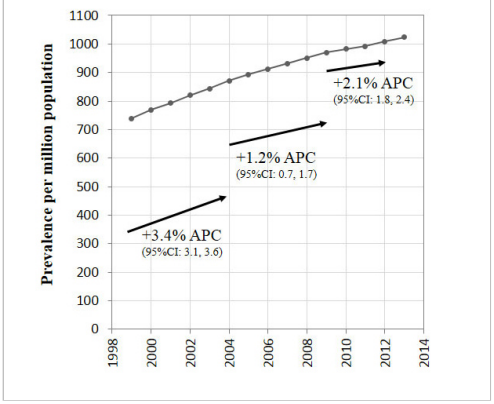

Figure 1.
Prevalent patients on renal replacement therapy in 1999-2013 [1] (APC - annual percentage change)

ually increasing incidence of pre-emptive kidney transplantation (KT) was observed, from 3.5 pmp in 1999 to 8.1 pmp in 2013. The group of hemodialysis patients represents the majority of the population of ESRD in subjects over 65 years (67.5%). Unlike the younger population where the biggest group of end stage kidney disease patients is after kidney transplantation. The transplant rate for all European countries included into the registry equals 30 pmp. The highest rate is in Croatia (60 pmp), the lowest in Ukraine (3 pmp). Poland is just above the average with the result of 31 pmp transplant rate [1].

Among kidney transplanted patients the vast majority received organ from deceased donor (74.7%, rate 32.2 pmp). Transplantation from living donation is more common in younger patients with ESRD (the group of patients under 65 year of age at the time of transplantation). Obviously kidney transplantation is an established method of renal failure treatment, it allows to restore homeostasis and thanks to this way of treatment patients are able to return to normal functioning in society. No doubts KT is the best method of ESRD therapy but it does not remain without drawbacks. Complications associated with the surgery procedure and later as a consequence of immunosuppressive therapy significantly affect the survival. However long-term survival benefit in ESRD population is observed regardless of age. The expected remaining lifetime of patients after kidney transplantation is about half longer than ones undergoing hemodialysis (Figure 2). Nevertheless the average life expectancy in transplant recipients is still reduced by 25-30% compared to general population [1].

Even though the dialysis patients and the ones after kidney transplantation comprises the visible expensive component of medical care it seems to be just like the tip of an iceberg. As it was mentioned at the beginning the largest group of patients with CKD, which carries increased risk of ESKD are not aware of any impairment of renal function.

Chronic kidney disease is the most common in elderly population. Deterioration in renal function with age was a subject of many studies in past years [2] [3] [4] [5] Researchers proved that in the elderly there glomerular filtration rate (GFR) and renal blood flow (RBF) reduces. The scale of decline in above mentioned parameters differ between individuals, however it was demonstrated that the average decline in glomerular filtration rate is estimated at 1 ml/min/1.73m² per year and effective renal plasma flow at about 8 ml/min/1.73m² per year [6]. Epidemiological studies attempt to answer the question what is the cause of worsening of the kidney function in

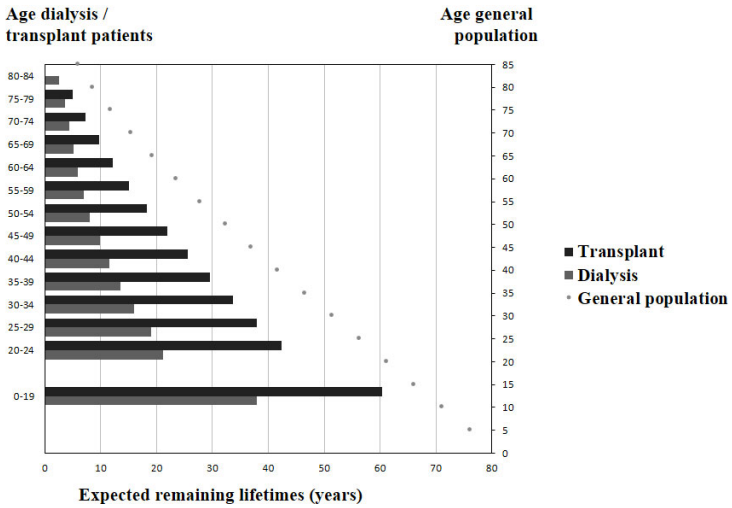

Figure 2.
Expected remaining lifetimes in the general population in 2010, and prevalent dialysis and transplant patients in 2012 and 2013 [1]

elderly. A various factors related the deterioration of kidney function can be enumerate, the ones connected with senility and those which are complications of concominant diseases. It includes: age at the genetic level in the form of telomere shortening and loss of mitochondria, then oxidative stress, glomerular hypertension and hyperfiltration, intrarenal activation of the renin angiotensin system, endothelial dysfunction with the loss of nitric oxide, next renal ischemia, accumulation of advance glycation products and chronic effect of uric acid. Even in the generally healthy elderly, kidneys themselves have features of senescence. Age affect kidneys in the form of nephrosclerosis or altering morphometric aspects. Under the term of nephrosclerosis the constellation of glomerulosclerosis, arteriosclerosis, tubular atrophy, and interstitial fibrosis is found [3]. More than two such changes will be present in light microscopy in 2.7% of group aged 18-29 years, in 44% of 50-59 year-olds and in 73% of population aged 70-77. It seems that age-related loss of renal function might be associated also with loss of renal mass. However decline in overall kidney volume seems to be present only in very elderly [3]. It was found that kidney weight decreases by approximately 19% in male and 9% in female in subjects aged 70-79 years in comparison to 20-29 year-olds individuals [2]. Considering partial sclerosis of glomeruli in many cases kidney volume is preserved by compensatory hypertrophy of intact nephrons which is again related to decreased glomerular density.

Based on the epidemiological study - PolNef, it was found that CKD occurs often in Polish population, in about 18.4% of subjects. Albuminuria appeared in almost 12% of the general population. The incidence of albuminuria was increasing with age [7]. Extremely valuable information about medical and also socio-economic aspects of aging in Polish population was brought by PolSenior study. PolSenior was the first multidisciplinary project focused on ageing in Poland performed in 2007-2011 [8]. Study involved 5695 individuals. On the basis of PolSenior results it was shown that the prevalence of chronic kidney disease in Polish population aged >65 years is 36.5% and eGFR<60ml/ml/1.73m^2 was observed in 27.7% of this population. In comparison in United State the prevalence of CKD in population age 60-69 is around 20% while in a group over 70 years old it is more than 45% [9]. In PolSenior as might be expected the prevalence of CKD increased with age. The CKD was more common in women than in men. The largest part of the population with impaired renal function was in stage 3 of CKD. Interesting conclusion was that 96.8% subjects were unaware about any impairment of renal function. The co-morbitity, in particular diabetes mellitus, arterial hypertension, prostate hyperplasia was clearly associated with decline in eGFR. Decreased glomerular filtration was also related to heart failure, coronary artery disease, occurrence of myocardial infarction and stroke. Albuminuria was observed in 25% individuals over 65 years old. Albumin-creatinine-ratio (ACR) >300mg was present in 2.3% subjects. The incidence of ACR <300mg increased with age and was significantly higher in men than in women aged > 65 years. What to expect albuminuria occurred more frequently in patients with diabetes. It was also associated with nephrolithiasis, failure and medical history of stroke [10]. Results were comparable in women and men.

Not only coexisting disease must be taken into account when analyzing the frequency of occurrence of CKD. An equally important factor is the socioeconomic determinants. Fedewa et. al showed that low income and low income communities are a risk factors of occurrence of end stage renal disease and that chronic kidney disease progression in independently linked to patients socioeconomic status. All cause-mortality in CKD patients was the highest in low income black race population [11]. Crews et. al observed that low socioeconomic status is strictly correlation with occurrence of CKD in African Americans. This correlation was not found in whites [12]. In PolSenior study the correlation between responders' education and the presence of chronic kidney disease was demonstrated. Researchers noted the highest prevalence of CKD among subjects with no education (55.8%), and the lowest in a group with vocational education (33.9%). What interesting not smoking and lower alcohol consumption were related to higher frequency of CKD. It was also valid for those with no regular physical activity. Results were similar for men and women [8].

Conclusions

Chronic kidney disease is a rather common condition in the elderly. It is found up to 30-40% in this population. PolSenior Study showed that CKD in Polish population was more frequent among elderly urban dwellers, non-smokers, alcohol abstinents and low physical activity. Only in women higher educational status was related to the lower risk of CKD. Potentially modifiable factors like health-related behaviours, comorbid conditions, and health-care access, contribute substantially to the association between low socioeconomic status and CKD. Lower socioeconomic status might lead to poorer self- management and thus greater complications from diabetes or arterial hypertension. Socioeconomic factors seems to be a suitable target for interventions at the national and supranational level aimed at reducing prevalence of CKD.

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