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EPIDEMIOLOGY OF CHRONIC KIDNEY DISEASE AND COMORBID ILLNESS IN HOSPITALIZED GERIATRIC PATIENTS

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EPIDEMIOLOGY OF CHRONIC KIDNEY DISEASE AND COMORBID ILLNESS IN HOSPITALIZED GERIATRIC PATIENTS (Abstract): **Background and aims**: The number of older people in Europe is expanding. Although chronic kidney disease (CKD) becomes more common with increasing age, data concerning epidemiology of CKD in older people are scarce, especially in Eastern Europe countries. In the current analysis, we aimed to fill the gap on CKD epidemiology in older people from Romania, by describing a large population of hospitalized geriatric patients. **Material and methods:** In this retrospective cohort study we included all patients aged ≥ 65 years hospitalized in the Geriatric Department of "Dr. C. I. Parhon" Hospital from Iași, Romania, between 2012 – 2022. CKD was identified as decreased estimated glomerular filtration rate (<60 mL/min/1.73 m^2) according to CKD-EPI equation. Investigated comorbid conditions included diabetes mellitus, hypertension/hypertensive heart disease, coronary artery disease, congestive heart failure, atrial fibrillation, chronic respiratory failure and anemia. **Results**: 3,563 geriatric patients (59.2% females) were hospitalized between 2012-2022. 3116 patients (87.4% of the total population) had a serum creatinine assay. Among these patients, the prevalence of CKD using the CKD-EPI equation was 38%. We found an unequal annually distribution between the number of patients with a diagnosis of CKD according to electronic health records and the number of patients with estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2. 86,7% of the patients with eGFR < 60 mL/min/1.73 m^2 had at least 2 comorbidities. Only 2,4% of the patients with eGFR < 60 mL/min had no other chronic condition. **Conclusions:** In Romanian older hospitalized patients, the prevalence of individuals with eGFR <60 mL/min/1.73 m2 is higher than previous reports from our country. In geriatric adults, CKD is not an isolated entity, and the burden of cardiovascular comorbid illness is high. **Keywords**: EPIDEMIOLOGY, CHRONIC KIDNEY DISEASE, COMORBID ILLNESS, HOSPITALIZED GERIATRIC PATIENTS.

The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines define chronic kidney disease (CKD) as abnormalities of kidney structure or function, present for > 3 months, with implications for health (1). The classification of CKD requires the determination of the cause of CKD, glomerular filtration rate (GFR) category (G1-G5) and albuminuria category (A1-A3). By standardizing the definition and staging of CKD, data on CKD burden have grown. Globally, in 2017, there were 697.5 million

cases of all-stage CKD, for a global prevalence of 9.1 % (2). However, based on a meta-analysis of 100 studies (roughly 7 million patients), the global CKD prevalence could be as high as 13.4 %, with a prevalence of CKD stages G3 to G5 of 10.6 % (3). In Europe, estimates of CKD prevalence indicate a regional variation across 27 countries that ranges from 3.31% in Norway to 17.3 % in Germany (4). Regional disparities in CKD burden arise from differences in geographic area and ethnicity, issues related to GFR estimation (e.g., type of equation used) ore one-off testing assessments in large-scale reports.

Although the growing CKD burden parallels the expanding proportion of older individuals, data concerning epidemiology of CKD in older people are scarce, especially in Eastern Europe countries. These patients have multiple chronic conditions that need to be correctly quantified for guiding risk stratification and subsequent management. Previously, European Renal Best Practice (ERBP) guidelines shed some light on management of older patients with advanced CKD, by stimulating implementation of validated tools for predicting the most important risks, death and progression to end-stage renal disease (ESRD). When comparing the above - mentioned risks, it is important to note that in older people with CKD, death is a more likely event than progression to ESRD, even at severe reductions in GFR (5).

The starting point for an effective strategy of screening for CKD consists of increasing awareness of the true burden of the disease and utilization of simple laboratory tests (serum creatinine to estimate GFR and proteinuria) to identify CKD in people at risk. A systematic review suggested that screening for CKD is cost effective in people with diabetes and hypertension, the two most common causes of CKD worldwide (6). From a practical point of view, early identification of CKD in people at-risk is beneficial in the primary care settings if the programs are associated with treatment strategies. However, there are no current evidence-based recommendations regarding the frequency of screening in people at risk of CKD.

In the current analysis, we aimed to fill the gap on CKD epidemiology in older people from Romania, by describing a large population of hospitalized geriatric patients. We found only two other analysis (7, 8) published in that last twelve years that investigated the prevalence of CKD in the adult population of Romania, none with focus on geriatric patients.

MATERIAL AND METHODS

In this retrospective cohort study, we included all patients aged ≥ 65 years hospitalized in the Geriatric Department of "Dr. C. I. Parhon" Hospital from Iasi, Romania, between 2012 - 2022.

This Geriatric Unit covers the entire North-East region of the country, so patients are representative for a population of almost 4 million people. We selected for our analysis those in which serum creatinine was performed. In this population, we calculated the estimated glomerular filtration rate (eGFR) by using CKD-EPI equation. Based on the KDIGO definition and classification of CKD (1), we first divided our population into "no CKD" (defined as eGFR > 60 mL/min/1.73 m2) and "CKD" (eGFR < 60 mL/min/1.73 m^2). The CKD group was further classified based on GFR category in G3a (45-59 mL/min/1.73 m^2),

G3b (30-44 mL/min/1.73 m^2), G4 (15-29 mL/min/1.73 m2) and G5 (<15 mL/min/1.73 m^2). Investigated comorbid conditions included diabetes mellitus, hypertension/hypertensive heart disease, coronary artery disease, congestive heart failure, atrial fibrillation, chronic respiratory failure and anemia. We investigated the distribution of these comorbidities in the entire geriatric population and in the CKD group.

RESULTS

In the Geriatric Unit from "Dr. C. I. Parhon" Hospital from Iasi between 2012 and 2022, there were 3,563 patients hospitalized with an age greater than 65 years old at admission - 1,453 (40.8%) male, 2,110 (59.2%) female.

Out of the total patients > 65 years old (3,563), only 3116 patients had at least one serum creatinine value determined between 2012 and 2022 (a total of 7954 values determined). Taking into account the first creatinine value corresponding to an estimated GFR of < 60 mL/min/1.73 m^2 (CKD-EPI), there were 1,187 individual patients with an eGFR <60 mL/min/1.73 m^2, corresponding to a prevalence of 38%. Mean age of patients with eGFR < 60 mL/min/1.73 m^2 was 79 years and gender distribution was unequal (63.4% females).

We explored the distribution of the primary or secondary diagnosis of Chronic Kidney Disease (N18, N19) according to International Classification of Diseases (ICD 10) in the hospital records. The difference in numbers between patients with eGFR < 60 mL/min and patients with CKD (ICD 10) as primary or secondary diagnosis is shown in first figure.

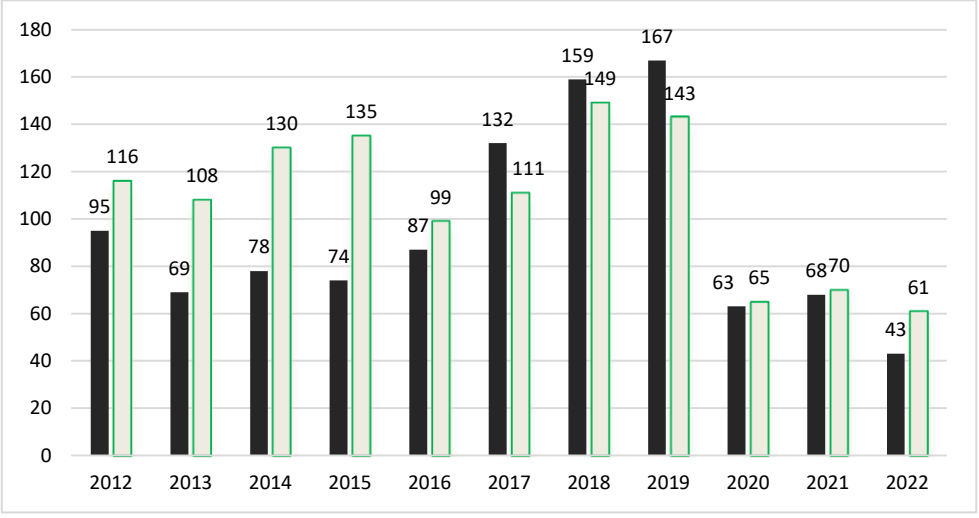

Fig. 1. Number of patients with eGFR < 60 mL/min (white) and patients with CKD diagnosis (ICD 10) (black), between 2012-2022.

Out of the 3,116 patients with at least one serum creatinine assessment, 1,655 patients had 2 or more creatinine values during different hospitalizations. Taking into account the first hospitalization of each patient during the 10-year interval, we found that 758 patients

had an eGFR < 60 mL/min of first assessment in the Geriatric Unit. The distribution of eGFR according to CKD-EPI for the first admission is described in first table.

TABLE I.
The distribution of eGFR according to CKD-EPI for the first admission

eGFR	Women	Men	Total
>90 mL/min	359	382	741
60-89 mL/min	1035	582	1617
45-59 mL/min	284	180	464
30-44 mL/min	163	71	234
15-29 mL/min	35	19	54
<15 mL/min	6		6
Total	**1,882**	**1,234**	**3,116**

According to ICD 10 diagnosis, in patients with eGFR < 60 mL/min, the most frequent comorbidity was heart failure (28.9%), followed by hypertension (20.7%), ischemic heart disease (15.2%), diabetes (10.5%), chronic respiratory disease (7.5%), atrial fibrillation (5.3%) and anemia (6.3%) (tab. II).

The distribution of patients with eGFR < 60 mL/min stratified by the number of comorbidities showed that 86.7% had ≥ 2 comorbidities. The largest CKD subgroup was the one that associated 3 comorbidities (315 patients, 31.5%), followed by two subgroups that had 2 comorbidities (249 patients, 24.9%), respectively 4 comorbidities (189 patients, 18.9%). Only a minority of patients with eGFR < 60 mL/min (24 adults, 2.4%) had no other chronic condition (tab. III).

TABLE II.
Distribution of main comorbidities according to eGFR

Comorbidities	eGFR>=60	eGFR<60	All patients (n= 3,116)
Heart failure	29.60%	28.90%	29.38%
Hypertension	21.10%	20.70%	21.00%
Ischemic heart disease	16.90%	15.20%	16.46%
Diabetes mellitus	8.30%	10.50%	8.90%
Chronic respiratory disease	8.30%	7.50%	8.12%
Atrial fibrillation	5.30%	5.30%	5.30%
Anemia	4%	6.30%	4.64%
Other comorbidities	6.40%	5.60%	6.21%

TABLE III.
The number of concurrent comorbidities in patients with eGFR < 60 mL/min.

Number of concurrent comorbidities	Percent of patients with eGFR < 60
0	2.40%
1	10.90%
2	24.90%
3	31.50%
4	18.90%
5	8.00%
6	2.90%
7	0.30%
8	0.10%

DISCUSSION

The analysis of this representative sample of the Romanian older hospitalized patients shows that the prevalence of eGFR <60 mL/min/1.73 m^2 is high (38 %). The identified prevalence is higher than the one previously reported by Mota *et al.* (8). In that study, researchers analyzed data from 2,717 Romanian adults and found an overall age- and sex-adjusted prevalence of CKD of 6.74%. The prevalence of CKD increased with age from 3.69 % in the 20–39-year age group to 14.35 % in the 60–79-year age group. In the Kidney Early Evaluation Program (KEEP) and National Health and Nutrition Examination Survey (NHANES) in the United States, which included more than 32,000 patients aged at least 65 years, the prevalence of CKD was 44% (9), which is similar to our findings.

In a systematic review of 26 population-based studies, the median prevalence of CKD was 7.2% in people aged ≥ 30 years, but it ranged from 23.4% to 35.8% in people aged ≥ 64 years (10).

An important section of our analysis was the comparison between the number of patients with a diagnosis of CKD according to International Classification of Diseases (ICD 10) and the number of patients with eGFR < 60 mL/min/1.73 m^2, using CKD-EPI equation. This comparison was made for each of the 11 years of the observation period. In the first 4 years of the selected period (2012-2015), there seems to be a greater difference between the CKD diagnosis and patients with eGFR < 60 mL/min/1.73 m^2, with less patients labeled as having CKD (fig. 1). This suggests that there might have been an under-recording of CKD diagnoses in healthcare records. The accuracy of CKD diagnosis using electronic health records (EHR) ultimately depends on the integration and interpretation of data by healthcare providers and the quality of the healthcare system's electronic records.

The difference between the CKD diagnosis and patients with eGFR < 60 mL/min/1.73 m2 is smaller starting from 2016 onward, with a slightly higher number of patients with CKD diagnosis. The number of patients with eGFR < 60

mL/min/1.73 m^2 is constantly increasing until 2019. Since the beginning of the COVID-19 pandemic (2020), both categories of patients are significantly decreased. The main reason could be the significant initial restrictions in the referrals to the Geriatric Unit, followed probably by an increased reluctance for inpatient vs outpatient care in the elderly population.

When examining the number of patients with eGFR < 60 mL/min/1.73 m^2, we can conclude that during the 11-year period, the prevalence has increased from 758/3116 patients (low eGFR on first admission) to 1,187/3,116 patients (taking into account the eGFR progression).

In our study, cardio-vascular pathology was a frequent characteristic of the population, with approximately one third of the patients that have heart failure and one fifth associating hypertension. The extent of the investigated comorbidities was similar across eGFR groups (>/= 60 mL/min *vs.* < 60 mL/min).

We also emphasized that in older adults, CKD is not an isolated entity, which makes the caring for these patients challenging, especially if we add the negative impact of other superimposed geriatric syndromes like frailty and cognitive decline.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. KDIGO 2023 clinical practice guideline for the evaluation and management of chronic kidney disease /https://kdigo.org/wp-content/uploads/2017/02/KDIGO-2023-CKD-Guideline-Public-Review-Draft_5-July-2023.pdf
2. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2020; 395: 709-733.
3. Hill NR, Fatoba ST, Oke JL, *et al*. Global Prevalence of Chronic Kidney Disease - A Systematic Review and Meta-Analysis. *PLoS One* 2016; 11: e0158765.
4. Brück K, Stel VS, Gambaro G, *et al*. CKD Prevalence Varies across the European General Population. *J Am Soc Nephrol* 2016; 27: 2135-2147 / doi: 10.1681/ASN.2015050542.
5. Prakash S, O'Hare AM. Interaction of aging and chronic kidney disease. *Semin Nephrol* 2009; 29(5): 497-503.
6. Komenda P, Ferguson TW, Macdonald K, *et al.* Cost-effectiveness of primary screening for CKD: a systematic review. *Am J Kidney Dis* 2014; 63: 789-797.

7. Cepoi V, Onofriescu M, Segall L, Covic A. The prevalence of chronic kidney disease in the general population in Romania: a study on 60,000 persons. *International urology and nephrology* 2012; 44: 213-220.
8. Moţa E, Popa SG, Moţa M, *et al*. Prevalence of chronic kidney disease and its association with cardio-metabolic risk factors in the adult Romanian population: the PREDATORR study. *International urology and nephrology* 2015; 47: 1831-1838.
9. Stevens LA, Li S, Wang C, *et al*. Prevalence of CKD and comorbid illness in elderly patients in the United States: results from the Kidney Early Evaluation Program (KEEP). *Am J Kidney Dis* 2010; 55(3 Suppl 2): S23-33.
10. Zhang QL, Rothenbacher D. Prevalence of chronic kidney disease in population-based studies: systematic review. *BMC Public Health* 2008; 8: 117 / doi: 10.1186/1471-2458-8-117.